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NEWS 1		Web Page for STN Seminar Schedule - N. America
NEWS 2	AUG 15	CAOLD to be discontinued on December 31, 2008
NEWS 3	OCT 07	EPFULL enhanced with full implementation of EPC2000
NEWS 4	OCT 07	Multiple databases enhanced for more flexible patent number searching
NEWS 5	OCT 22	Current-awareness alert (SDI) setup and editing enhanced
NEWS 6	OCT 22	WPIDS, WPINDEX, and WPIX enhanced with Canadian PCT Applications
NEWS 7	OCT 24	CHEMLIST enhanced with intermediate list of pre-registered REACH substances
NEWS 8	NOV 21	CAS patent coverage to include exemplified prophetic substances identified in English-, French-, German-, and Japanese-language basic patents from 2004-present
NEWS 9	NOV 26	MARPAT enhanced with FSORT command
NEWS 10	NOV 26	MEDLINE year-end processing temporarily halts availability of new fully-indexed citations
NEWS 11	NOV 26	CHEMSAFE now available on STN Easy
NEWS 12	NOV 26	Two new SET commands increase convenience of STN searching
NEWS 13	DEC 01	ChemPort single article sales feature unavailable
NEWS 14	DEC 12	GBFULL now offers single source for full-text coverage of complete UK patent families
NEWS 15	DEC 17	Fifty-one pharmaceutical ingredients added to PS

NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 17:28:22 ON 21 DEC 2008

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 17:28:35 ON 21 DEC 2008
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Property values tagged with IC are from the ZIC/VINITI data file
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STRUCTURE FILE UPDATES: 19 DEC 2008 HIGHEST RN 1087349-26-5
DICTIONARY FILE UPDATES: 19 DEC 2008 HIGHEST RN 1087349-26-5

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TSCA INFORMATION NOW CURRENT THROUGH July 5, 2008.

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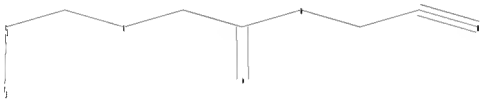
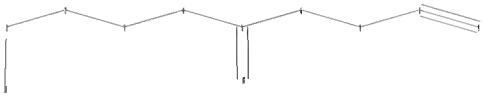
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=>
Uploading C:\Program Files\Stnexp\Queries\10518692\Struc 1.str





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chain bonds :
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exact/norm bonds :
1-2 1-11 2-3 3-4 5-6 5-13 6-7 8-9
exact bonds :
4-5 7-8

G1:Cb,Cy,Hy

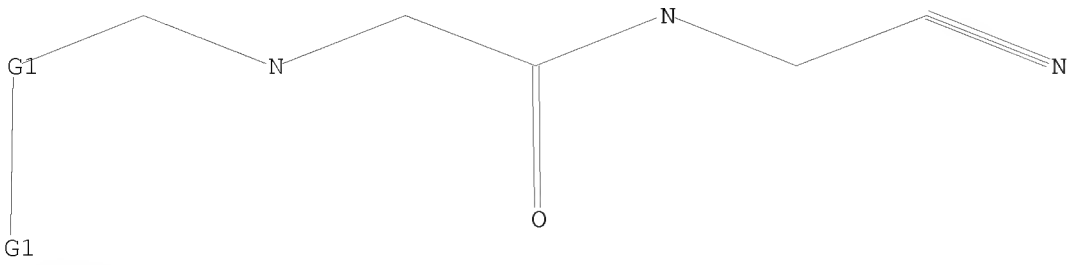
Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:CLASS
11:CLASS 13:CLASS

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS

10581692.trn

L1 STR



G1 Cb,Cy,Hy

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SEARCH INITIATED 17:29:04 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      828 TO ITERATE

100.0% PROCESSED      828 ITERATIONS                              17 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        14834 TO    18286
PROJECTED ANSWERS:              93 TO      587

L2           17 SEA SSS SAM L1

=> l1 full
FULL SEARCH INITIATED 17:29:07 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    17618 TO ITERATE

100.0% PROCESSED    17618 ITERATIONS                             411 ANSWERS
SEARCH TIME: 00.00.01

L3          411 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              178.36     178.57

FILE 'CAPLUS' ENTERED AT 17:29:11 ON 21 DEC 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 21 Dec 2008 VOL 149 ISS 26
FILE LAST UPDATED: 19 Dec 2008 (20081219/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/legal/infopolicy.html

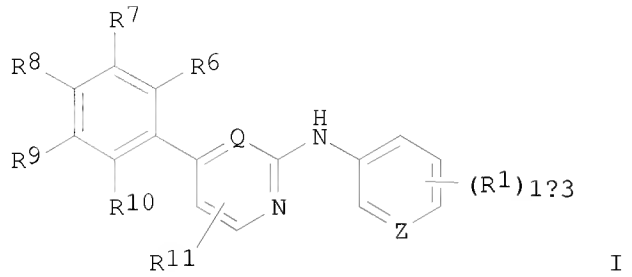
=> l3
L4 38 L3

=> d ibib abs hitstr 1-38

L4 ANSWER 1 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:1127907 CAPLUS
DOCUMENT NUMBER: 149:402373
TITLE: (Phenylamino)pyrimidine derivatives as protein kinases inhibitors and their preparation, pharmaceutical compositions and use in the treatment of diseases
INVENTOR(S): Burns, Christopher John; Donohue, Andrew Craig; Feutrill, John Thomas; Ngygen, Thao Lien Thi; Wilks, Andrew Frederick; Zeng, Jun
PATENT ASSIGNEE(S): Cytopia Research Pty Ltd, Australia
SOURCE: PCT Int. Appl., 104pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008109943	A1	20080918	WO 2008-AU339	20080312
W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2007-894264P P 20070312
US 2007-16252P P 20071221
OTHER SOURCE(S): MARPAT 149:402373
GI



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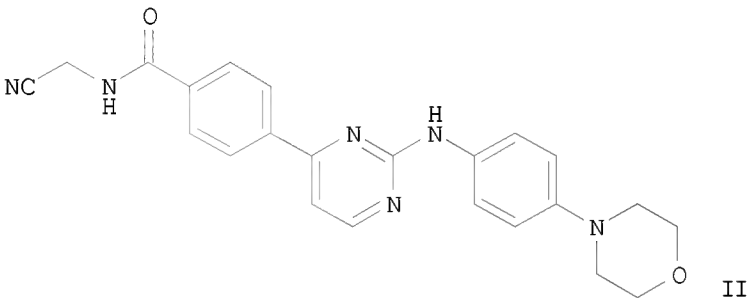
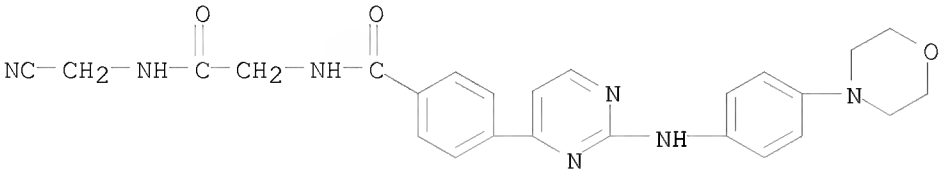


II

AB The invention relates to (phenylamino)pyrimidine derivs. of formula I, which are inhibitors of protein kinases including JAK kinases. In particular, the compds. are selective for JAK2 kinases. The kinase inhibitors can be used in the treatment of kinase associated diseases such as immunol. and inflammatory diseases including organ transplants; hyperproliferative diseases including cancer and myeloproliferative diseases; viral diseases; metabolic diseases; and vascular diseases. Compds. of formula I wherein Q and Z are independently N and CR1; R1 is H, halo, R2, OR2, OH, R4, OR4, CN, CF3, (CH2)1-3-N(R2)2, NO2, etc.; R2 is (un)substituted C1-4 alkyl and (un)substituted C1-4 alkylene where up to two carbon atoms can be optionally replaced with CO, NH and derivs., CONH and derivs., S, SO2 and O; R4 is NH2 and derivs., (un)substituted (thio)morpholino, (un)substituted thiomorpholino-1-oxide, etc.; R6-R10 are independently H, RxCN, halo, (un)substituted C1-4 alkyl, OR1, CO2R1, N(R1)2, NO2, CON(R1)2, etc.; Rx is absent, (un)substituted C1-6 alkylene where up to two carbon atoms can be optionally replaced with CO, NSO2R1, CONH and derivs., S, SO2 and O; R11 is H, halo, (un)substituted C1-4 alkyl, OR2, CO2R2, CN, CON(R1)2 and CF3; and their enantiomers, prodrugs and pharmaceutically acceptable salts thereof, are claimed. Example compound II was prepd.via Suzuki coupling of 4-(ethoxycarbonyl)phenylboronic acid with 2,4-dichloropyrimidine followed by amination with 4-morpholinoaniline, hydrolysis and amidation with aminoacetonitrile. All the invention compds. were evaluated for their protein kinases inhibitory activity. From the assay, it was determined that II exhibited an IC50 value of < 5 μM against JAK2.

IT 1056635-32-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(drug candidate; preparation of (phenylamino)pyrimidine derivs. as protein kinase inhibitors useful in treatment of diseases)
RN 1056635-32-5 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

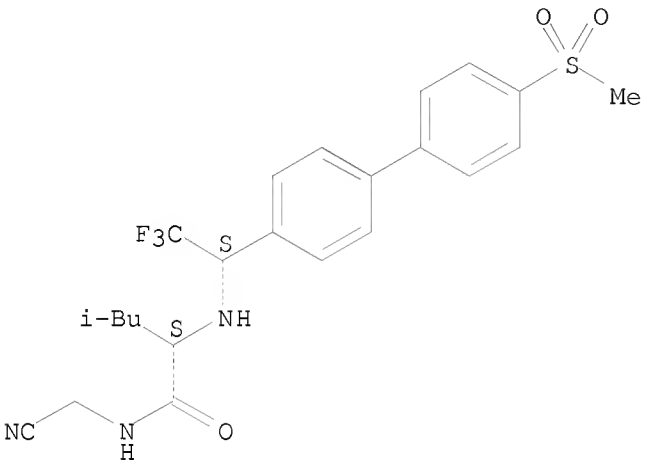


REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:151744 CAPLUS
DOCUMENT NUMBER: 148:393709
TITLE: The discovery of odanacatib (MK-0822), a selective inhibitor of cathepsin K
AUTHOR(S): Gauthier, Jacques Yves; Chauret, Nathalie; Cromlish, Wanda; Desmarais, Sylvie; Duong, Le T.; Falgueyret, Jean-Pierre; Kimmel, Donald B.; Lamontagne, Sonia; Leger, Serge; LeRiche, Tammy; Li, Chun Sing; Masse, Frederic; McKay, Daniel J.; Nicoll-Griffith, Deborah A.; Oballa, Renata M.; Palmer, James T.; Percival, M. David; Riendeau, Denis; Robichaud, Joel; Rodan, Gideon A.; Rodan, Sevgi B.; Seto, Carmai; Therien, Michel; Truong, Vouy-Linh; Venuti, Michael C.; Wesolowski, Gregg; Young, Robert N.; Zamboni, Robert; Black, W. Cameron
CORPORATE SOURCE: Merck Frosst Centre for Therapeutic Research, Kirkland, QC, H9H 3L1, Can.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2008), 18(3), 923-928
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 148:393709
AB Odanacatib is a potent, selective, and neutral cathepsin K inhibitor which was developed to address the metabolic liabilities of the Cat K inhibitor L-873724. Substituting P1 and modifying the P2 side chain led to a metabolically robust inhibitor with a long half-life in preclin. species. Odanacatib was more selective in whole cell assays than the published Cat K inhibitors balicatib and relacatib. Evaluation in dermal fibroblast culture showed minimal intracellular collagen accumulation relative to less selective Cat K inhibitors.
IT 603139-12-4, L-873724 603141-69-1 603142-15-0 847361-57-3 922138-48-5 1016226-43-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discovery of odanacatib, a selective inhibitor of cathepsin K)
RN 603139-12-4 CAPLUS

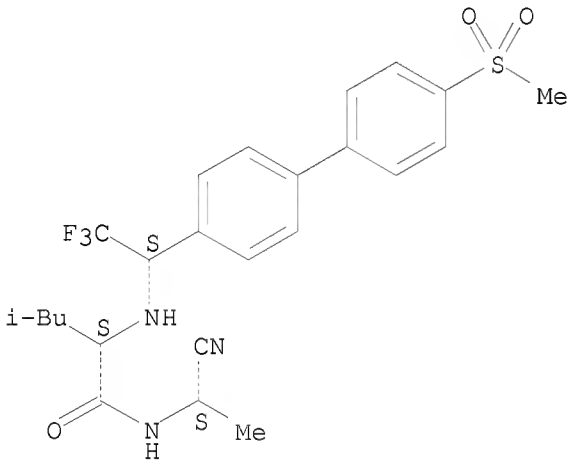
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



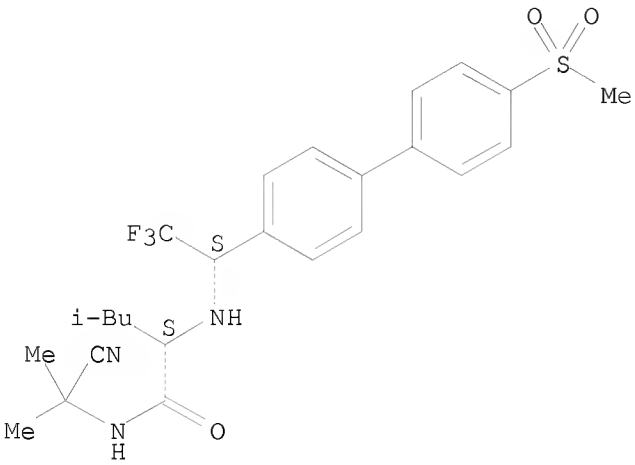
RN 603141-69-1 CAPLUS
CN Pentanamide, N-[(1S)-1-cyanoethyl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



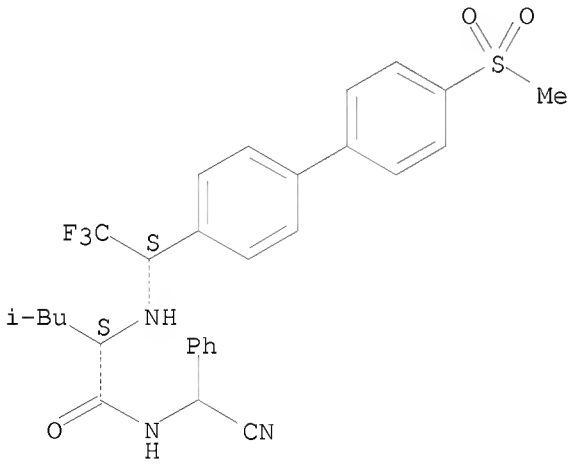
RN 603142-15-0 CAPLUS
CN Pentanamide, N-(1-cyano-1-methylethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



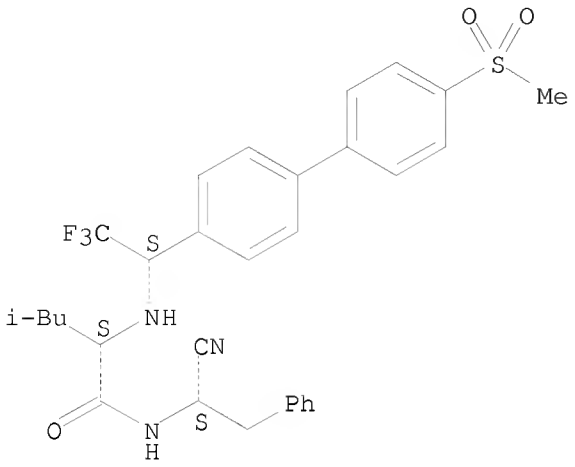
RN 847361-57-3 CAPLUS
CN Pentanamide, N-(cyanophenylmethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



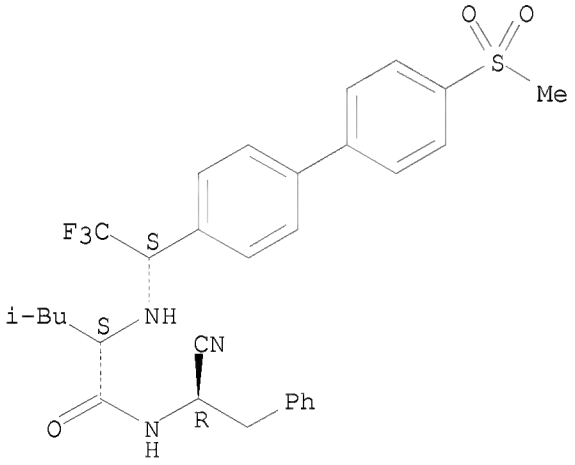
RN 922138-48-5 CAPLUS
CN Pentanamide, N-[(1S)-1-cyano-2-phenylethyl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 1016226-43-9 CAPLUS
CN Pentanamide, N-[(1R)-1-cyano-2-phenylethyl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)-(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:47494 CAPLUS
DOCUMENT NUMBER: 148:299774
TITLE: Effect of cathepsin K inhibitor basicity on in vivo off-target activities
AUTHOR(S): Desmarais, Sylvie; Black, W. Cameron; Oballa, Renata; Lamontagne, Sonia; Riendeau, Denis; Tawa, Paul; Duong, Le Thi; Pickarski, Maureen; Percival, M. David
CORPORATE SOURCE: Departments of Biochemistry and Molecular Biology, Merck Frosst Centre for Therapeutic Research,

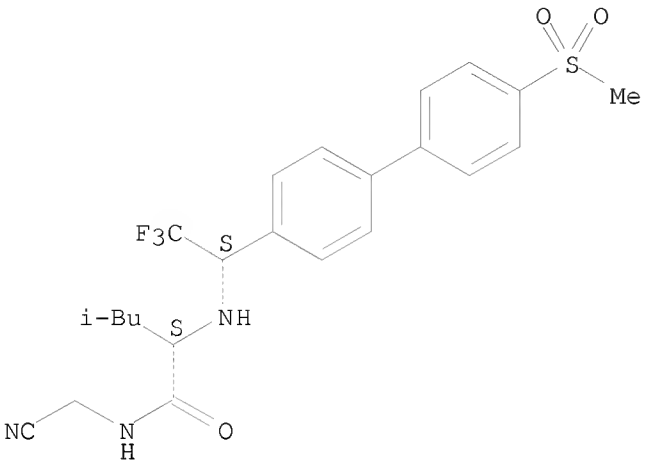
Kirkland, QC, Can.
SOURCE: Molecular Pharmacology (2008), 73(1), 147-156
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cathepsin K is a lysosomal cysteine protease that is a pharmacol. target for the treatment of osteoporosis. Previous studies showed that basic, lipophilic cathepsin K inhibitors are lysosomotropic and have greater activities in cell-based assays against cathepsin K, as well as the physiol. important lysosomal cysteine cathepsins B, L, and S, than expected based on their potencies against these isolated enzymes. Long-term administration of the basic cathepsin K inhibitors N-(1-(((cyanomethyl)amino)carbonyl)cyclohexyl)-4-(2-(4-methylpiperazin-1-yl)-1,3-thiazol-4-yl)benzamide (L-006235) and balicatib to rats at a supratherapeutic dose of 500 mg/kg/day for 4 wk resulted in increased tissue protein levels of cathepsin B and L but had no effect on cathepsin B and L message. This is attributed to the inhibitor engagement of these off-target enzymes and their stabilization to proteolytic degradation No such increase in these tissue cathepsins was detected at the same dose of L-873724, a potent nonbasic cathepsin K inhibitor with a similar off-target profile, although all three inhibitors provided similar plasma exposures. Using an activity-based probe, 125I-BIL-DMK, in vivo inhibition of cathepsins B, L, and S was detected in tissues of mice given a single oral dose of L-006235 and balicatib, but not in mice given L-873724. In each case, similar tissue levels were achieved by all three compds., thereby demonstrating the in vivo cathepsin selectivity of L-873724. In conclusion, basic cathepsin K inhibitors demonstrate increased off-target cysteine cathepsin activities than their nonbasic analogs and potentially have a greater risk of adverse effects associated with inhibition of these cathepsins.

IT 603139-12-4, L-873724
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of cathepsin K inhibitor basicity on in vivo off-target activities)

RN 603139-12-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

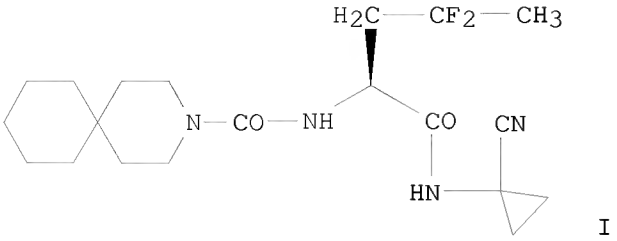
L4 ANSWER 4 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1392046 CAPLUS
DOCUMENT NUMBER: 148:34023
TITLE: Synthesis and testing of spirocyclic amino acid nitrile derivs. as cathepsin cysteine protease inhibitors
INVENTOR(S): Schudok, Manfred; Wagner, Michael; Bauer, Armin; Kohlmann, Anna
PATENT ASSIGNEE(S): Sanofi-Aventis, Fr.
SOURCE: PCT Int. Appl., 153pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007137738	A1	20071206	WO 2007-EP4550	20070523

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: DE 2006-102006025630A 20060601
OTHER SOURCE(S): MARPAT 148:34023
GI



I

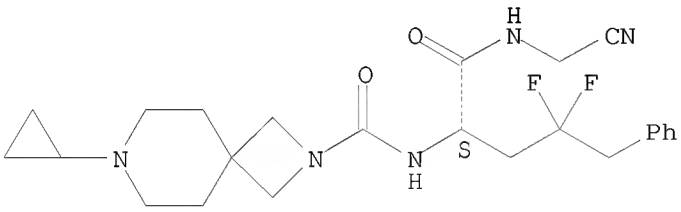
AB Title compds., e.g. (I), were prepared and tested as cathepsin cysteine protease inhibitors for use in the treatment of disease, e.g. bone diseases or cancers. Thus, Cbz-Asp-OMe (Cbz = benzyloxycarbonyl protecting group) was reacted with oxalyl chloride to give Me (S)-2-benzyloxycarbonylamino-3-chlorocarbonyl propionate; this intermediate was then treated with CuBr, LiBr, and MeMgCl to give Me (S)-2-benzyloxycarbonylamino-4-oxopentanoate, which was fluorinated using BAST. The resulting intermediate was Cbz-deprotected and converted to the 2-isocyanato compound, which was then reacted with 3-aza-spiro[5.5]undecane to give the intermediate acid (II). II was coupled with 1-amino-1-cyclopropyl nitrile to give the product I (43% of theor. yield). In in vitro tests using human Cathepsins K, B, and S, I had Ki (inhibition constant) values of 1.8, 46, and 3.2 nM, resp.

IT 1003564-72-4P 1003564-74-6P 1003564-75-7P
1003564-76-8P
RL: PAC (Pharmacological activity); PRPH (Prophetic); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of)

RN 1003564-72-4 CAPLUS

CN 2,7-Diazaspiro[3.5]nonane-2-carboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3,3-difluoro-4-phenylbutyl]-7-cyclopropyl- (CA INDEX NAME)

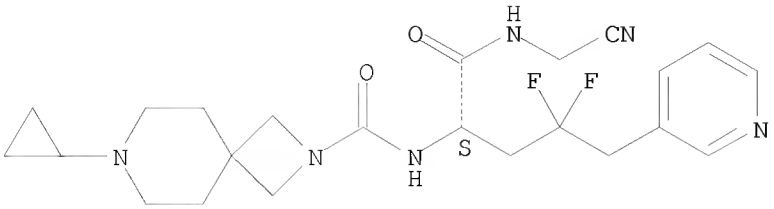
Absolute stereochemistry.



RN 1003564-74-6 CAPLUS

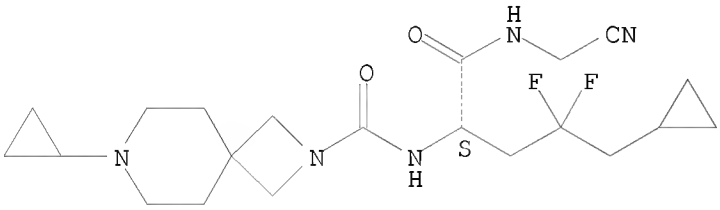
CN 2,7-Diazaspiro[3.5]nonane-2-carboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3,3-difluoro-4-(3-pyridinyl)butyl]-7-cyclopropyl- (CA INDEX NAME)

Absolute stereochemistry.



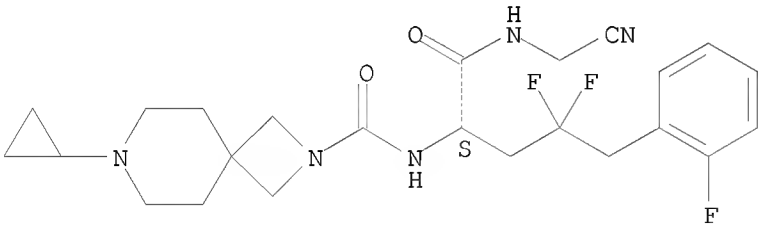
RN 1003564-75-7 CAPLUS
CN 2,7-Diazaspiro[3.5]nonane-2-carboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-4-cyclopropyl-3,3-difluorobutyl]-7-cyclopropyl- (CA INDEX NAME)

Absolute stereochemistry.



RN 1003564-76-8 CAPLUS
CN 2,7-Diazaspiro[3.5]nonane-2-carboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3,3-difluoro-4-(2-fluorophenyl)butyl]-7-cyclopropyl- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:862465 CAPLUS
DOCUMENT NUMBER: 147:377563
TITLE: The identification of potent, selective, and bioavailable cathepsin S inhibitors
AUTHOR(S): Gauthier, Jacques Yves; Black, W. Cameron; Courchesne, Isabelle; Cromlish, Wanda; Desmarais, Sylvie; Houle, Robert; Lamontagne, Sonia; Li, Chun Sing; Masse, Frederic; McKay, Daniel J.; Ouellet, Marc; Robichaud, Joel; Truchon, Jean-Francois; Truong, Vouy-Linh; Wang, Qingping; Percival, M. David

CORPORATE SOURCE: Departments of Medicinal Chemistry, Merck Frosst Centre for Therapeutic Research, Kirkland, QC, H9R 4P8, Can.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2007), 17(17), 4929-4933
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 147:377563

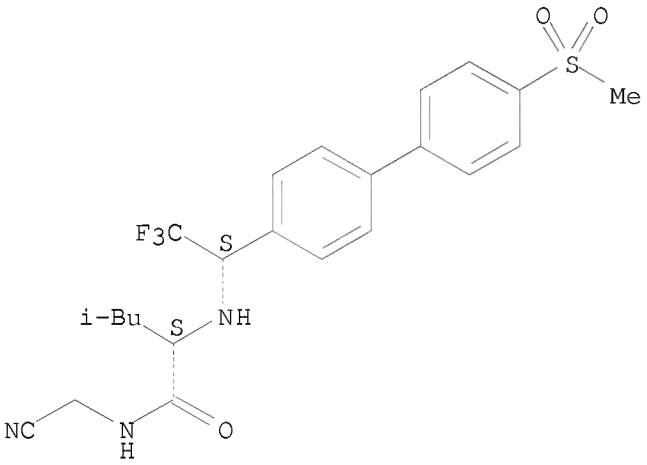
AB Highly potent, selective, and bioavailable inhibitors of human, mouse, or rat cathepsin S are described. The key structural features combine a sulfonyl moiety attached to a large group in P2 and a small substituent in P3.

IT 603139-12-4, L 873724
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(identification of potent, selective, and bioavailable cathepsin S inhibitors)

RN 603139-12-4 CAPLUS

CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

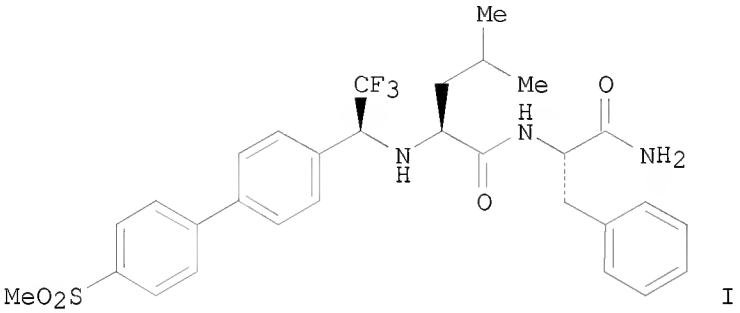
Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:746507 CAPLUS
DOCUMENT NUMBER: 147:314168
TITLE: Primary amides as selective inhibitors of cathepsin K
AUTHOR(S): Leger, Serge; Bayly, Christopher I.; Black, W. Cameron; Desmarais, Sylvie; Falgueyret, Jean-Pierre; Masse, Frederic; Percival, M. David; Truchon, Jean-Francois
CORPORATE SOURCE: Merck Frosst Centre for Therapeutic Research, Pointe-Claire-Dorval, QC, H9R 4P8, Can.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2007),

17(15), 4328-4332
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 147:314168
GI



I

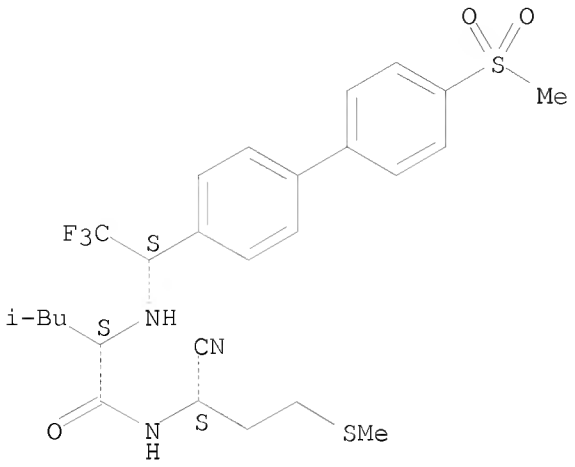
AB The nitrile warhead used in a series of cathepsin K inhibitors can be replaced by a less electrophilic primary amide. The accompanying loss of potency can be partially recovered by introducing a substituent α to the amide. The potency gain resulting from this addition is not achieved with the nitrile derivs. due to a different geometry of the cysteine adduct in the enzyme active site. This study led to the identification of the primary amide (I), which is an inhibitory substrate, with an IC50 of 10 nM against cathepsin K and excellent selectivity vs. the other cathepsins.

IT 603141-70-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(6primary amides as selective inhibitors of cathepsin K)

RN 603141-70-4 CAPLUS

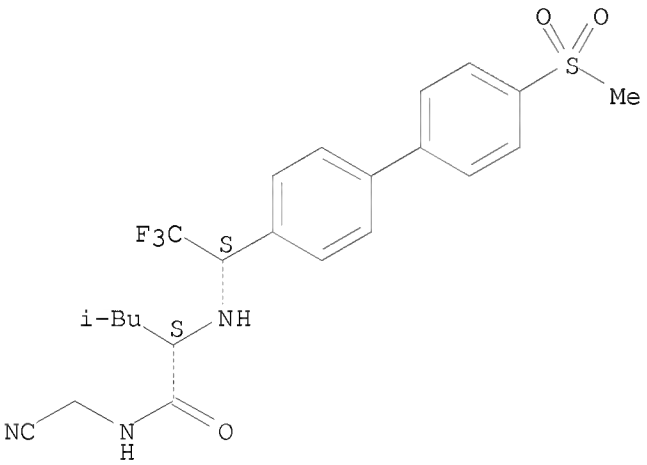
CN Pentanamide, N-[(1S)-1-cyano-3-(methylthio)propyl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)-(CA INDEX NAME)

Absolute stereochemistry.



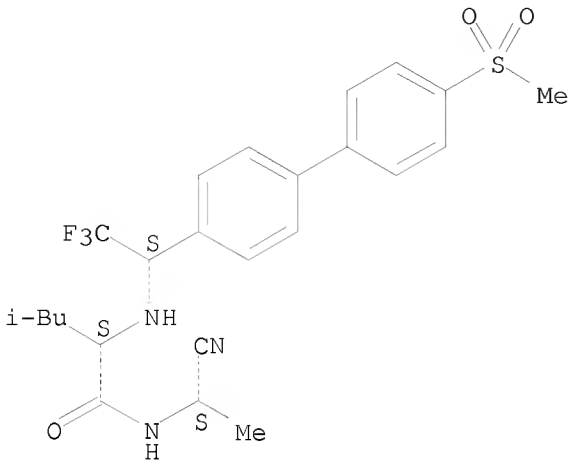
IT 603139-12-4P 603141-69-1P 922138-48-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(primary amides as selective inhibitors of cathepsin K)
RN 603139-12-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



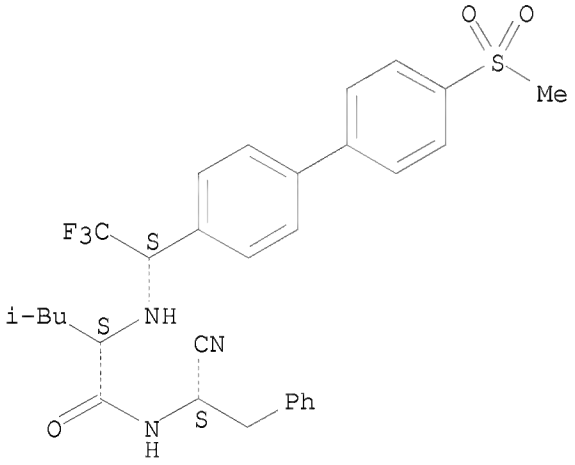
RN 603141-69-1 CAPLUS
CN Pentanamide, N-[(1S)-1-cyanoethyl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 922138-48-5 CAPLUS
CN Pentanamide, N-[(1S)-1-cyano-2-phenylethyl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)-(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:330406 CAPLUS
DOCUMENT NUMBER: 146:358859
TITLE: Preparation of isoxazoline-substituted benzamide derivatives as insecticides, acaricides, and parasiticides
INVENTOR(S): Mita, Takeshi; Kikuchi, Takamasa; Mizukoshi, Takashi; Yaosaka, Manabu; Komoda, Mitsuaki
PATENT ASSIGNEE(S): Nissan Chemical Industries, Ltd., Japan
SOURCE: U.S. Pat. Appl. Publ., 172pp., Cont.-in-part of Appl.

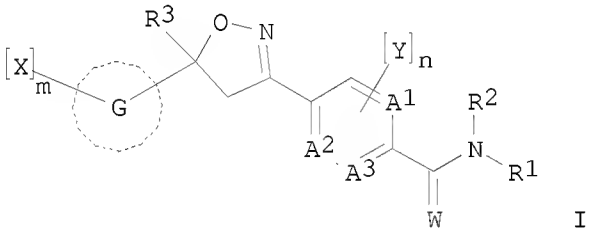
No. PCT/JP2005/004268.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20070066617	A1	20070322	US 2006-514921	20060905
WO 2005085216	A1	20050915	WO 2005-JP4268	20050304

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2004-61749 A 20040305
JP 2004-200119 A 20040707
WO 2005-JP4268 A2 20050304

OTHER SOURCE(S): MARPAT 146:358859
GI

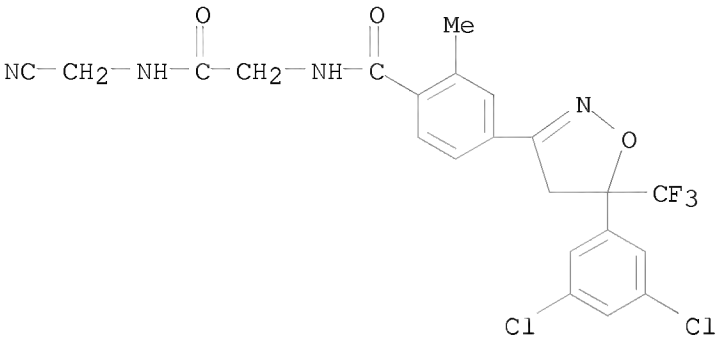


I

AB The title compds. I [A1-A3 = C, N; ring G = benzene ring, N-containing 6-membered aromatic heterocyclic ring, furan ring, etc.; W = O, S; X = halo, cyano, haloalkyl, etc.; Y = halo, cyano, nitro, alkyl, etc.; R1, R2 = H, cyano, alkyl, etc.; or R1 and R2 may together form alkylene and thus R1R2N may form 3-8 membered ring; R3 = halo, cyano, alkyl, etc.; m = 0-5; n = 0-4], useful as insecticides, acaricides, and parasiticides, were prepared Thus, 4-[5-(3,5-dichlorophenyl)-5-trifluoromethyl-4,5-dihydroisoxazol-3-yl]-2-nitro-N-(2-pyridylmethyl)benzoic acid amide was prepared in a multi-step process starting from 4-bromo-3-nitrobenzaldehyde and hydroxylamine. Compds. I were tested against various insects (data given).

IT 930107-32-7P
RL: AGR (Agricultural use); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of isoxazoline-substituted benzamide derivs. as insecticides, acaricides, and parasiticides)

RN 930107-32-7 CAPLUS
CN Benzamide, N-[2-[(cyanomethyl)amino]-2-oxoethyl]-4-[5-(3,5-dichlorophenyl)-4,5-dihydro-5-(trifluoromethyl)-3-isoxazolyl]-2-methyl- (CA INDEX NAME)



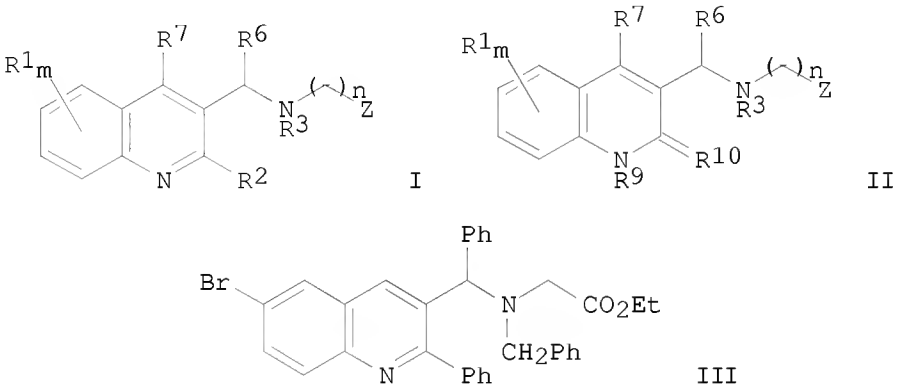
L4 ANSWER 8 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:143490 CAPLUS
DOCUMENT NUMBER: 146:229195
TITLE: Preparation of quinoline derivatives as antibacterial agents
INVENTOR(S): Guillemont, Jerome Emile Georges; Lancois, David Francis Alain; Pasquier, Elisabeth Therese Jeanne; Andries, Koenraad Jozef Lodewijk Marcel; Koul, Anil
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 109pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007014885	A1	20070208	WO 2006-EP64656	20060726
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006274918	A1	20070208	AU 2006-274918	20060726
CA 2614981	A1	20070208	CA 2006-2614981	20060726
EP 1912948	A1	20080423	EP 2006-777972	20060726
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, RS				

IN 2008DN00668	A	20080711	IN 2008-DN668		20080124
MX 200801219	A	20080324	MX 2008-1219		20080125
US 20080182855	A1	20080731	US 2008-996786		20080125
KR 2008031973	A	20080411	KR 2008-704457		20080225
NO 2008001008	A	20080227	NO 2008-1008		20080227
CN 101273016	A	20080924	CN 2006-80035175		20080324
PRIORITY APPLN. INFO.:			EP 2005-106962	A	20050728
			WO 2006-EP64656	W	20060726

OTHER SOURCE(S): MARPAT 146:229195

GI



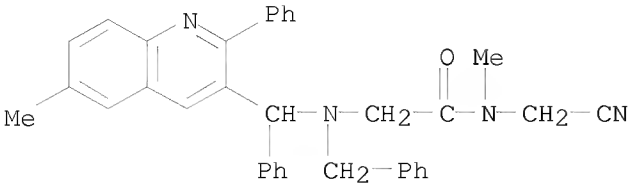
I II III

AB Use of a compound for the manufacture of a medicament for the treatment of a bacterial infection provided that the bacterial infection is other than a Mycobacterial infection, said compound being a compound of formula I & II (Z = -X-NR4R5 or -CO2R8; R1 = cyano, halo(alkyl), hydroxy, etc.; R2 = H, aryl, mercapto, etc.; R3 = alkyl, aryl(alkyl), mono- or di-alkylaminoalkyl or heterocyclyl(alkyl); R4, R5 = independently H, (alkoxy)alkyl, aryl, etc., or R4R5N = heterocyclyl; R6 = (un)substituted aryl or heterocyclyl; R7 = H, halo, alkyl, aryl or heterocyclyl; R8 = saturated hydrocarbon radical; m = 0-4; n = 1-3), a pharmaceutically acceptable acid or base addition salt, a quaternary amine, a stereochem. isomeric form, a tautomeric form or a N-oxide form thereof. For example, III was provided in a multi-step synthesis starting from the reaction of 5-bromo-1H-indole-2,3-dione with 1,3-diphenyl-1-propanone. I showed antibacterial activity in Microtitre plate assay.

IT 924631-78-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinoline derivs. for treatment of bacterial infection)

RN 924631-78-7 CAPLUS

CN Acetamide, N-(cyanomethyl)-N-methyl-2-[[(6-methyl-2-phenyl-3-quinolinyl)phenylmethyl](phenylmethyl)amino]- (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

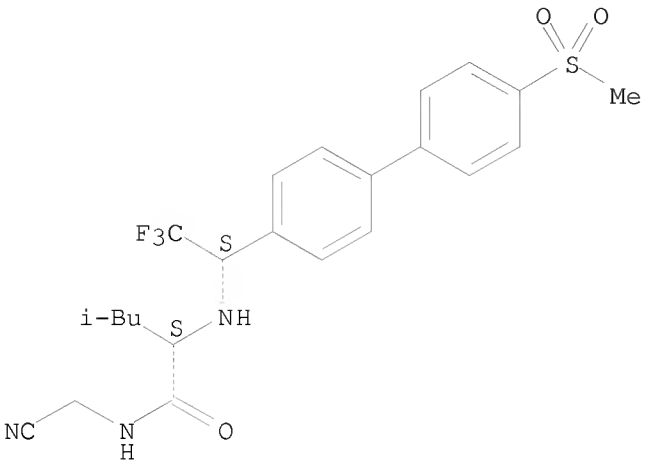
L4 ANSWER 9 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:129940 CAPLUS
DOCUMENT NUMBER: 146:350583
TITLE: A generally applicable method for assessing the electrophilicity and reactivity of diverse nitrile-containing compounds
AUTHOR(S): Oballa, Renata M.; Truchon, Jean-Francois; Bayly, Christopher I.; Chauret, Nathalie; Day, Stephen; Crane, Sheldon; Berthelette, Carl
CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Frosst Centre for Therapeutic Research, Kirkland, QC, H9H 3L1, Can.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2007), 17(4), 998-1002
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Nitrile-based inhibitors of cathepsin K have been known for some time and mechanism-of-action studies have demonstrated that cysteinyl proteases interact with nitriles in a reversible fashion. Three main classes of nitrile-containing inhibitors have been published in the cathepsin K field: (i) cyanamides, (ii) aromatic nitriles, and (iii) aminoacetonitriles. A computational approach was used to calculate the theor. reactivities of diverse nitriles and this was found to correlate with their extent of reactivity with free cysteine. Moreover, there is a tentative link between high reactivity with cysteine and the potential to lead to irreversible covalent binding to proteins.

IT 603139-12-4 930575-91-0
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); BIOL (Biological study); PROC (Process)
(method for assessing electrophilicity and reactivity of diverse nitrile-containing compds.)

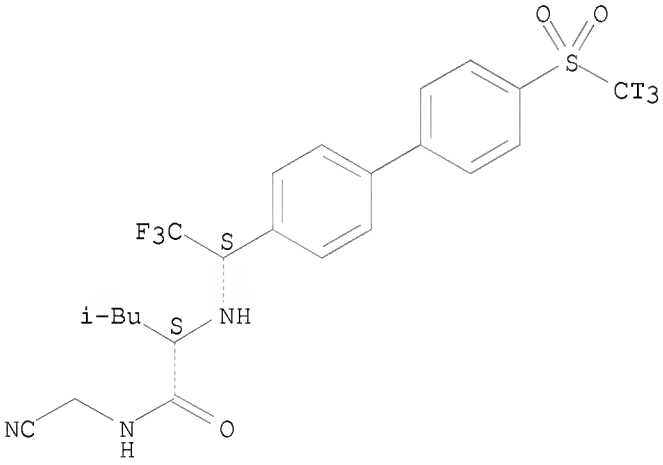
RN 603139-12-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 930575-91-0 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methyl-t3-sulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:113649 CAPLUS
DOCUMENT NUMBER: 146:177158
TITLE: Papain family cysteine protease inhibitors for the treatment of parasitic diseases
INVENTOR(S): Black, Cameron; Mellon, Christophe; Nicoll-Griffith, Deborah Anne; Oballa, Renata
PATENT ASSIGNEE(S): Merck Frosst Canada Ltd., Can.
SOURCE: PCT Int. Appl., 42pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007012180	A1	20070201	WO 2006-CA1216	20060724
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1909784	A1	20080416	EP 2006-761177	20060724
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
MX 200801207	A	20080324	MX 2008-1207	20080125
PRIORITY APPLN. INFO.:			US 2005-702455P P	20050726
			WO 2006-CA1216 W	20060724

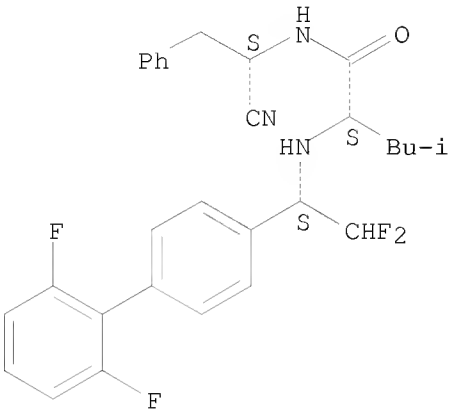
OTHER SOURCE(S): MARPAT 146:177158

AB The invention relates to the treatment of parasitic disease with inhibitors of the papain family cysteine proteases The parasitic diseases include toxoplasmosis, malaria, African trypanosomiasis, Chagas disease, leishmaniasis and schistosomiasis The invention also relate to the pharmaceutical compns. comprising a papain family cysteine protease inhibitor and another agent in the treatment for parasitic disease.

IT 922138-41-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(papain family cysteine protease inhibitors for treatment of parasitic diseases and combination with other agents)

RN 922138-41-8 CAPLUS
CN Pentanamide, N-[(1S)-1-cyano-2-phenylethyl]-2-[[(1S)-1-(2',6'-difluoro[1,1'-biphenyl]-4-yl)-2,2-difluoroethyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

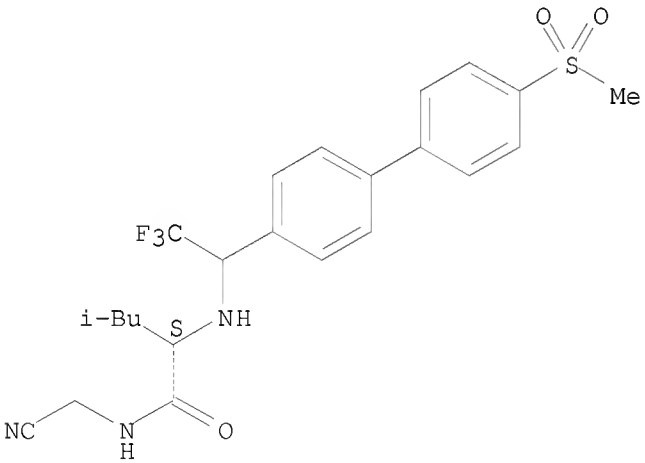


IT 603139-99-7P 603141-70-4P 603141-71-5P
847361-57-3P 922138-48-5P 922138-49-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(papain family cysteine protease inhibitors for treatment of parasitic diseases and combination with other agents)

RN 603139-99-7 CAPLUS

CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

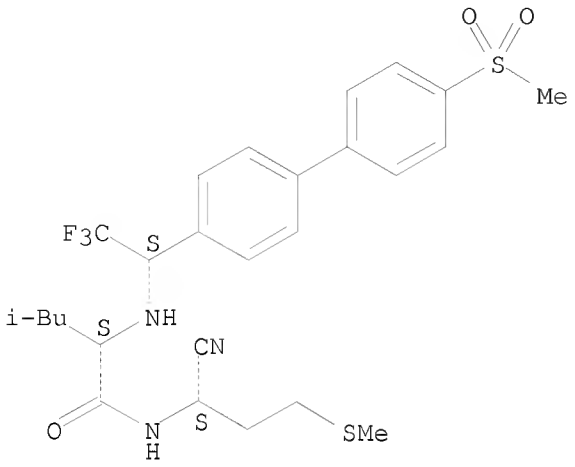
Absolute stereochemistry.



RN 603141-70-4 CAPLUS

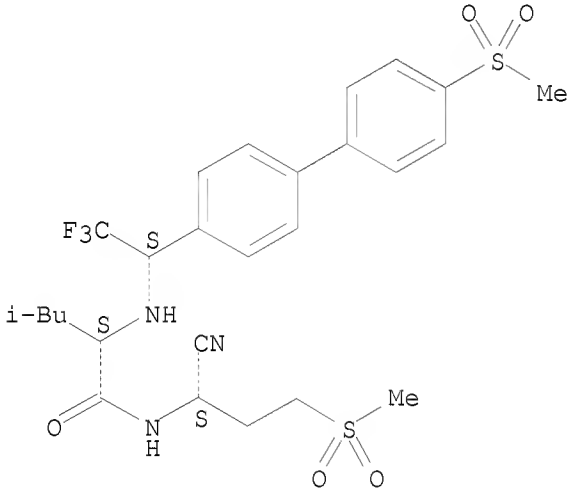
CN Pentanamide, N-[(1S)-1-cyano-3-(methylthio)propyl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



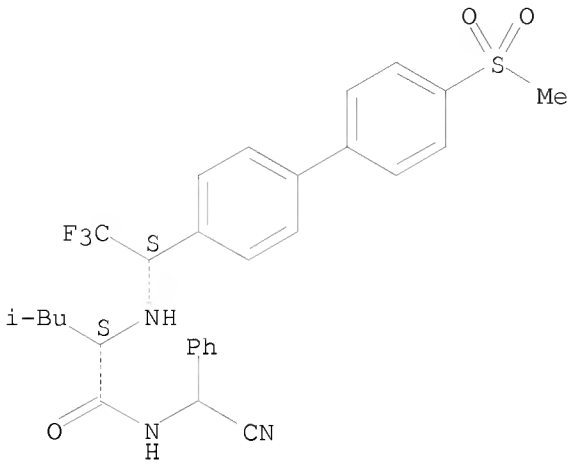
RN 603141-71-5 CAPLUS
CN Pentanamide, N-[(1S)-1-cyano-3-(methylsulfonyl)propyl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



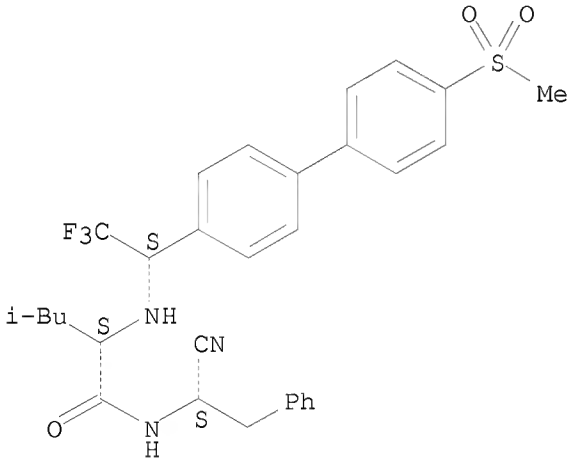
RN 847361-57-3 CAPLUS
CN Pentanamide, N-(cyanophenylmethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



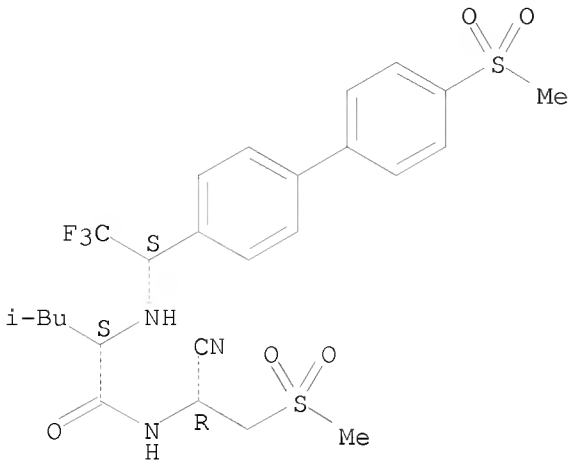
RN 922138-48-5 CAPLUS
CN Pentanamide, N-[(1S)-1-cyano-2-phenylethyl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



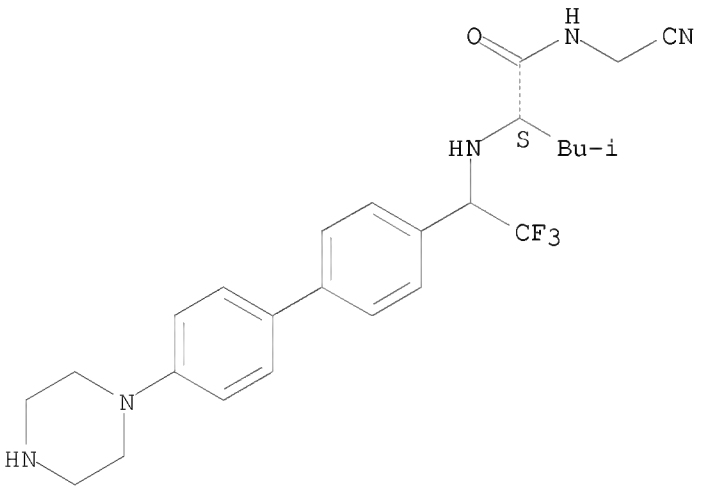
RN 922138-49-6 CAPLUS
CN Pentanamide, N-[(1R)-1-cyano-2-(methylsulfonyl)ethyl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 603139-07-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(papain family cysteine protease inhibitors for treatment of parasitic diseases and combination with other agents)
RN 603139-07-7 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4'-(1-piperazinyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:937462 CAPLUS
DOCUMENT NUMBER: 145:465162
TITLE: Substrate mapping and inhibitor profiling of falcipain-2, falcipain-3 and berghepain-2:

Implications for peptidase anti-malarial drug discovery

AUTHOR(S): Ramjee, Manoj K.; Flinn, Nicholas S.; Pemberton, Tracy P.; Quibell, Martin; Wang, Yikang; Watts, John P.

CORPORATE SOURCE: Amura Therapeutics Limited, Horizon Park, Comberton, CB3 7AJ, UK

SOURCE: Biochemical Journal (2006), 399(1), 47-57
CODEN: BIJOAK; ISSN: 0264-6021

PUBLISHER: Portland Press Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

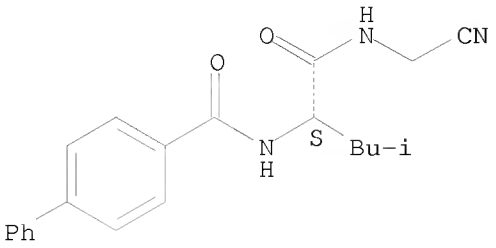
AB The Plasmodium falciparum cysteine peptidases FP-2 (falcipain-2) and FP-3 (falcipain-3), members of the papain-like CAC1 family, are essential hemoglobinases and are therefore potential antimalarial drug targets. To facilitate a rational drug discovery program, in the current study the authors analyzed the synthetic substrate and model inhibitor profiles of FP-2 and FP-3 as well as BP-2 (berghepain-2), an ortholog from the rodent parasite Plasmodium berghei. With respect to substrate catalysis, FP-2 exhibited a promiscuous substrate profile based around a consensus nonprimeside motif, FP-3 was somewhat more restricted and BP-2 was comparatively specific. Substrate turnover for FP-2 was driven by a basic or acidic P1 residue, whereas for FP-3 turnover occurred predominately through a basic P1 residue only, and for BP-2, turnover was again mainly through a basic P1 residue for some motifs and surprisingly a glycine in the P1 position for other motifs. Within these P1 binding elements, addnl. recognition motifs were observed with subtle nuances that switched substrate turnover on or off through specific synergistic combinations. The peptidases were also profiled against reversible and irreversible cysteine peptidase inhibitors. The results reiterated the contrasting kinetic behavior of each peptidase as observed through the substrate screens. The results showed that the substrate and inhibitor preferences of BP-2 were markedly different from those of FP-2 and FP-3. When FP-2 and FP-3 were compared to each other they also displayed similarities and some significant differences. In conclusion, the in vitro data highlights the current difficulties faced by a peptidase directed antimalarial medicinal chemical program where compds. need to be identified with potent activity against at least three peptidases, each of which displays distinct biochem. traits.

IT 225118-29-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substrate mapping and inhibitor profiling of falcipain-2, falcipain-3 and berghepain-2 and implications for peptidase anti-malarial drug discovery)

RN 225118-29-6 CAPLUS

CN [1,1'-Biphenyl]-4-carboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:735916 CAPLUS
DOCUMENT NUMBER: 145:159867
TITLE: Cathepsin K inhibitors for the treatment of obesity and obesity-related disorders
INVENTOR(S): Percival, Michael David
PATENT ASSIGNEE(S): Merck Frosst Canada Ltd., Can.
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

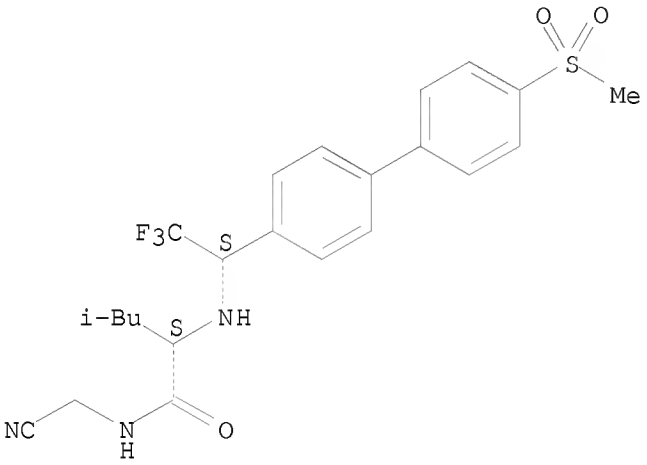
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006076796	A1	20060727	WO 2006-CA54	20060117
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1841419	A1	20071010	EP 2006-701777	20060117
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.: US 2005-644926P P 20050119
WO 2006-CA54 W 20060117
OTHER SOURCE(S): MARPAT 145:159867

AB The invention relates to the treatment of obesity, the treatment of obesity-related disorders, prevention of weight gain, prevention of weight regain or for weight maintenance, by the use of a cathepsin K inhibitor as active ingredient, alone or in conjunction with other anti-obesity agents. The invention also relates to pharmaceutical compns. comprising cathepsin K inhibitors as active ingredients, pharmaceutically acceptable carriers or excipients, and optionally one or more anti-obesity agents.

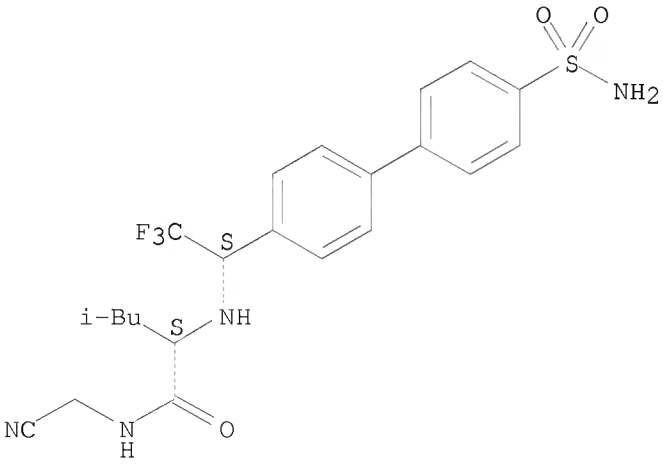
IT 603139-12-4 603139-13-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cathepsin K inhibitors for treatment of obesity and obesity-related disorders)
RN 603139-12-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 603139-13-5 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4'-(aminosulfonyl)[1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:733104 CAPLUS
DOCUMENT NUMBER: 145:159834
TITLE: Cathepsin K inhibitors and atherosclerosis
INVENTOR(S): Percival, Michael David
PATENT ASSIGNEE(S): Merck Frosst Canada Ltd., Can.
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2006076797	A1	20060727	WO 2006-CA55		20060117
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
EP 1841730	A1	20071010	EP 2006-701742		20060117
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR					
US 20080125442	A1	20080529	US 2007-795444		20070717
PRIORITY APPLN. INFO.:			US 2005-644938P	P	20050119
			WO 2006-CA55	W	20060117

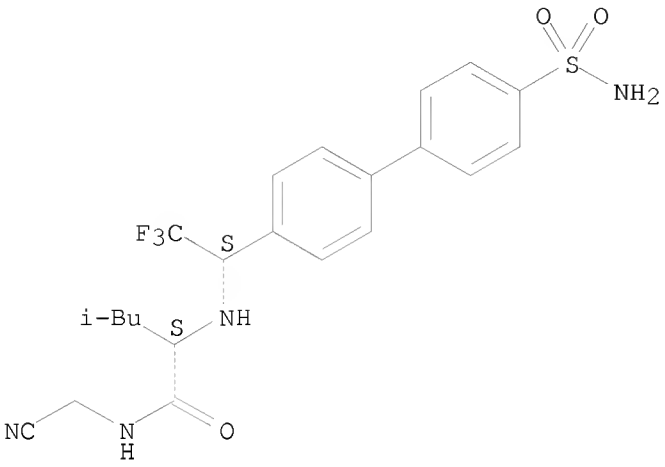
OTHER SOURCE(S): MARPAT 145:159834

AB This invention relates to a genus of compds., such as N1-(1-cyanocyclopropyl)-4-fluoro-N2-[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfinyl)-1,1'-biphenyl-4-yl]ethyl]-L-leucinamide or N-[1-[[(cyanomethyl)amino]carbonyl]cyclohexyl]-4-(4-propylpiperazin-1-yl)benzamide, which are inhibitors of cathepsin K. These compds. are useful for treating or preventing atherosclerosis and atherosclerotic cardiovascular disease.

IT 603139-13-5 603141-37-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cathepsin K inhibitors and treatment of atherosclerosis and atherosclerotic cardiovascular diseases and combination with other agents)

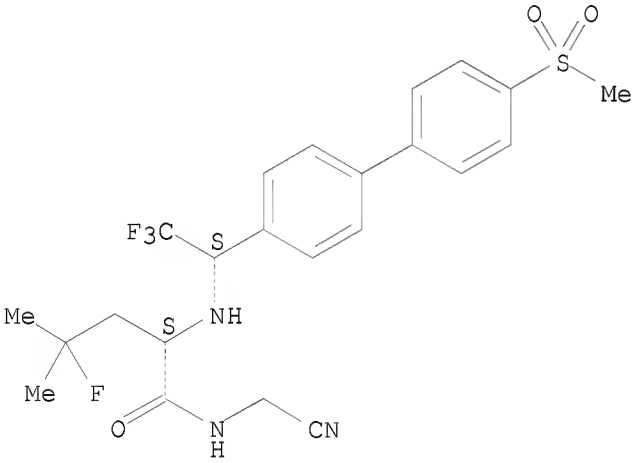
RN 603139-13-5 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4'-(aminosulfonyl)[1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 603141-37-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-fluoro-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

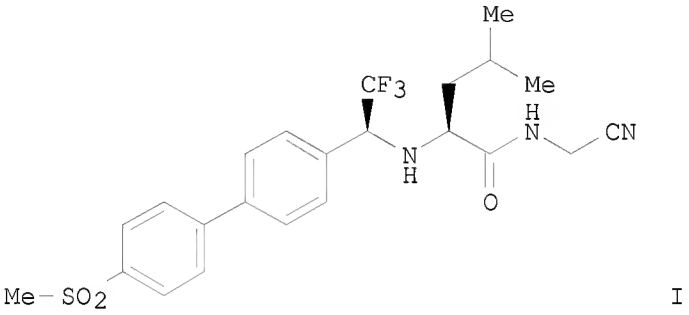
Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:413175 CAPLUS
DOCUMENT NUMBER: 145:124273
TITLE: Diastereoselective Aryllithium Addition to an α-Trifluoromethyl Imine. Practical Synthesis of a Potent Cathepsin K Inhibitor
AUTHOR(S): Roy, Amelie; Gosselin, Francis; O'Shea, Paul D.; Chen, Cheng-Y.
CORPORATE SOURCE: Department of Process Research, Merck Frosst Centre for Therapeutic Research, Kirkland, QC, H9H 3L1, Can.

SOURCE: Journal of Organic Chemistry (2006), 71(11), 4320-4323
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:124273
GI



I

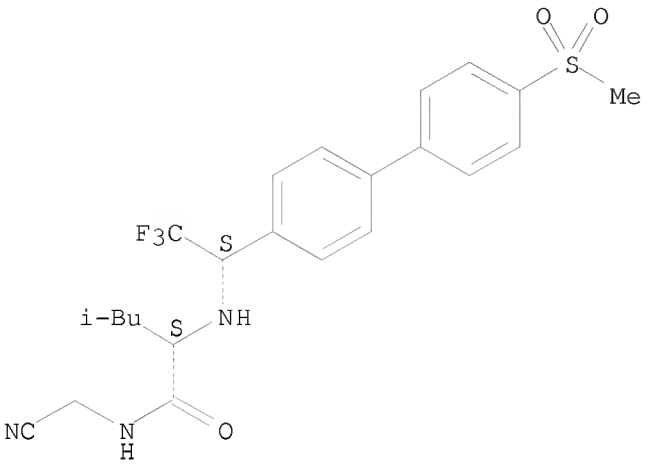
AB A practical, chromatog.-free synthesis of potent cathepsin K inhibitor I is described. The addition of 4-bromophenyllithium to an α-trifluoromethylimine derived from com. available (S)-leucinol was accomplished in a highly diastereoselective manner (97.6% de, 91% yield). Subsequent Suzuki cross-coupling afforded the biaryl derivative Oxidation of the alc. and sulfide functionalities led to the formation of carboxylic acid. Crystallization of the biaryl intermediate and the acid as its dicyclohexylamine salt gave excellent impurity rejection. The final amide coupling with com. available aminoacetonitrile hydrochloride afforded I in excellent purity (99.6A% by HPLC, 100% de, <3 ppm Pd, W, Cr).

IT 603139-12-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of a potent cathepsin K inhibitor by diastereoselective aryllithium addition to an α-trifluoromethyl imine)

RN 603139-12-4 CAPLUS

CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

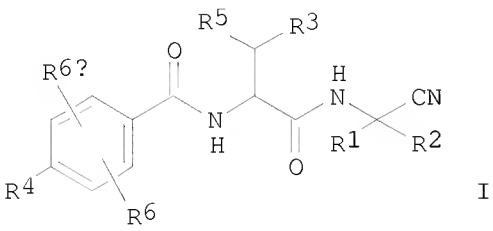
L4 ANSWER 15 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:367151 CAPLUS
DOCUMENT NUMBER: 144:412544
TITLE: Preparation of nitrile reversible inhibitors of cathepsin B
INVENTOR(S): Palmer, James T.; Rydzewski, Robert M.
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006042103	A2	20060420	WO 2005-US36127	20051005
WO 2006042103	A3	20060615		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-616417P P 20041005
OTHER SOURCE(S): CASREACT 144:412544; MARPAT 144:412544
GI



I

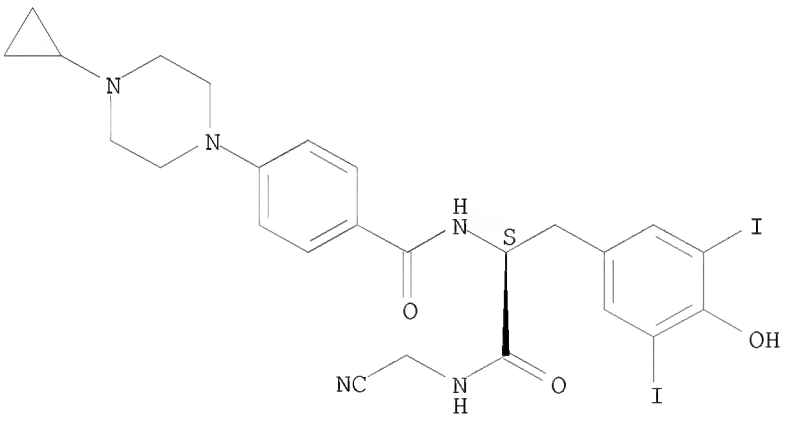
AB Nitriles [I; R1, R2 = haloalkyl, hydroxyalkyl; CR1R2 = cycloalkylene or heterocycloalkylene; R3 = heteroaryl, etc.; R4 = cycloalkylheterocycloalkyl; R5 = hydrogen, (halo)alkyl; R6, R6a = hydrogen, (un)substituted alkyl, (un)substituted alkenyl, alkoxy, cyano, halo, haloalkyl, haloalkoxy, alkylsulfonyl; e.g., N-[1-[N-(cyanomethyl)carbamoyl]-2-(4-hydroxy-3,5-diiodophenyl)ethyl]-4-(4-cyclopropylpiperazin-1-yl)benzamide], which demonstrate inhibition of cathepsin B and are useful in treating diseases, disorders, or syndromes mediated by cathepsin B, are prepared and I-containing pharmaceutical formulations presented.

IT 883743-80-4P 883743-86-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of reversible inhibitors of cathepsin B)

RN 883743-80-4 CAPLUS

CN Benzenepropanamide, N-(cyanomethyl)-α-[[4-(4-cyclopropyl-1-piperazinyl)benzoyl]amino]-4-hydroxy-3,5-diiodo-, (αS)- (CA INDEX NAME)

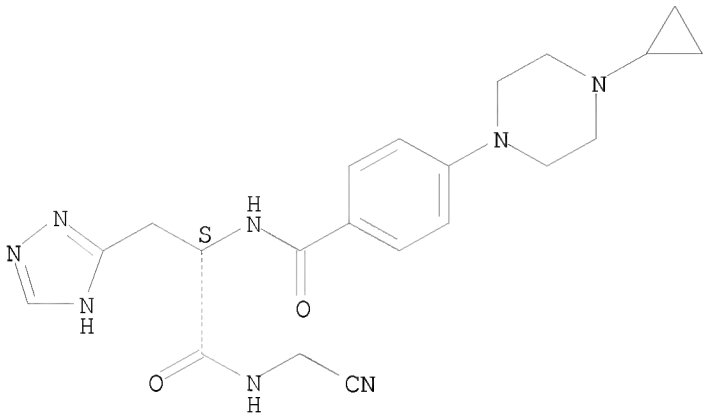
Absolute stereochemistry.



RN 883743-86-0 CAPLUS

CN 1H-1,2,4-Triazole-5-propanamide, N-(cyanomethyl)-α-[[4-(4-cyclopropyl-1-piperazinyl)benzoyl]amino]-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 16 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:298556 CAPLUS
DOCUMENT NUMBER: 144:350977
TITLE: Methods for the preparation of cyanomethyl peptide analogs useful as cysteine protease inhibitors
INVENTOR(S): Li, Jiayao
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006034004	A2	20060330	WO 2005-US33051	20050916
WO 2006034004	A3	20061123		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005287046	A1	20060330	AU 2005-287046	20050916
CA 2580065	A1	20060330	CA 2005-2580065	20050916
EP 1799645	A2	20070627	EP 2005-796693	20050916
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
CN 101068783	A	20071107	CN 2005-80038996	20050916
JP 2008513472	T	20080501	JP 2007-532479	20050916

BR 2005015470	A	20080722	BR 2005-15470		20050916
MX 200703118	A	20070524	MX 2007-3118		20070315
IN 2007DN02062	A	20070803	IN 2007-DN2062		20070316
US 20080114175	A1	20080515	US 2007-662933		20070316
KR 2007061877	A	20070614	KR 2007-708584		20070416
NO 2007001937	A	20070615	NO 2007-1937		20070416
PRIORITY APPLN. INFO.:			US 2004-610806P	P	20040917
			WO 2005-US33051	W	20050916

OTHER SOURCE(S): MARPAT 144:350977

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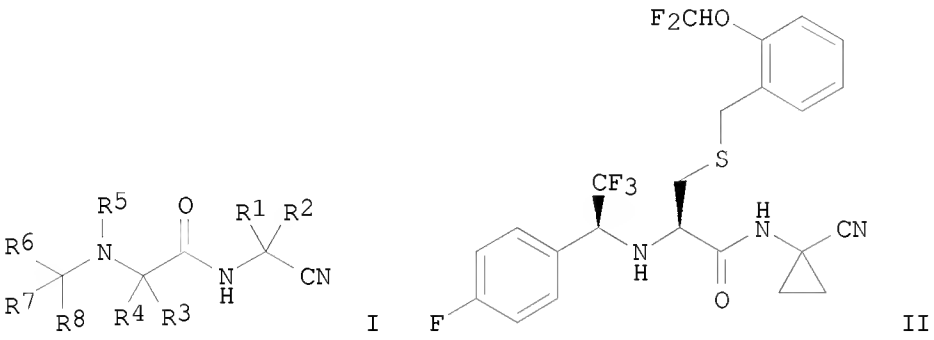


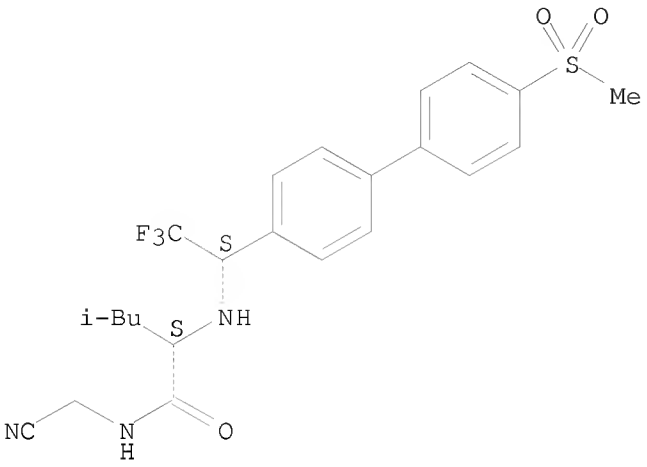
AB The present invention is directed to a novel process for preparing cyanomethyl peptide analogs I [R1 = H, alkyl; R2 = H, alkyl, haloalkyl, carboxyalkyl, alkoxycarbonylalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl, heterocyclylalkyl, CN, etc.; or R1 and R2 may form cycloalkyl or heterocycloalkyl ring; R3 = H, alkyl; R4 = alkyl, haloalkyl, cycloalkylalkyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, etc.; or R3 and R4 may form cycloalkyl ring; R5 = H, alkyl; R6 = (un)substituted cycloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl; R7 = haloalkyl, R8 = H, alkyl, haloalkyl] or pharmaceutically acceptable salts thereof, useful as cysteine protease inhibitors (no data). Thus, N-alkylation of S-(2-difluoromethoxybenzyl)-L-cysteine (preparation given) with 2,2,2-trifluoro-1-(4-fluorophenyl)ethyl triflate (preparation given), followed by S-oxidation and amidation with 1-aminocyclopropanecarbonitrile (preparation given) gave cyanocyclopropyl peptide analog II after column chromatog.

IT 603139-12-4P 603139-13-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(methods for the preparation of cyanomethyl peptide analogs useful as cysteine protease inhibitors)

RN 603139-12-4 CAPLUS

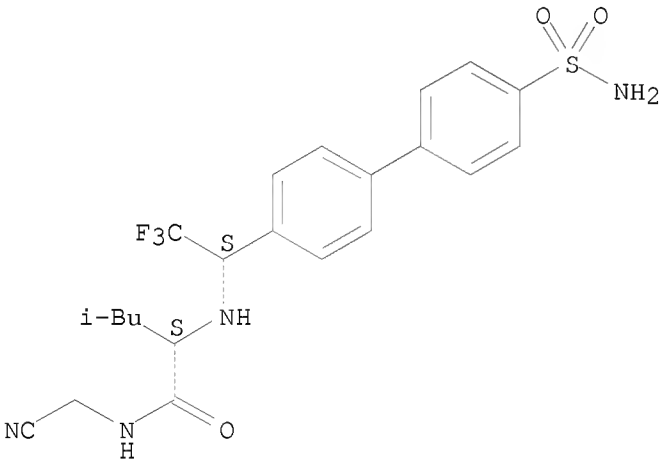
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 603139-13-5 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4'-(aminosulfonyl)[1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 17 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:228580 CAPLUS
DOCUMENT NUMBER: 144:460287
TITLE: Synthesis and in vitro evaluation of pseudosaccharinamine derivatives as potential elastase inhibitors
AUTHOR(S): Rode, Haridas; Koerbe, Stefanie; Besch, Anita; Methling, Karen; Loose, Jutta; Otto, Hans-Hartwig
CORPORATE SOURCE: Department of Pharmaceutical/Medicinal Chemistry, Institute of Pharmacy, Ernst-Moritz-Arndt-University, Greifswald, D-17489, Germany
SOURCE: Bioorganic & Medicinal Chemistry (2006), 14(8), 2789-2798

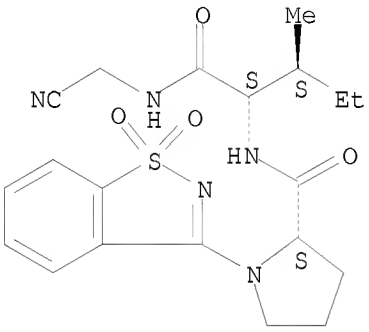
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:460287

AB Pseudosaccharinamine derivs. were evaluated for elastase inhibitory activity. Ester derivs. of pseudosaccharinamine displayed reversible and high inhibition of human leukocyte elastase (HLE) as compared to porcine pancreatic elastase (PPE). Cyanomethyl (2S,3S)-2-(1,1-dioxobenzo[d]isothiazol-3-ylamino)-3-methylpentanoate was found to inhibit HLE at Ki = 0.8 μM.

IT 886193-65-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and structure activity relationships of pseudosaccharinamine derivs. as elastase inhibitors)

RN 886193-65-3 CAPLUS
CN L-Isoleucinamide, 1-(1,1-dioxido-1,2-benzisothiazol-3-yl)-L-prolyl-N-(cyanomethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:188910 CAPLUS
DOCUMENT NUMBER: 144:403771
TITLE: Identification of a potent and selective non-basic cathepsin K inhibitor
AUTHOR(S): Li, Chun Sing; Deschenes, Denis; Desmarais, Sylvie; Falgueyret, Jean-Pierre; Gauthier, Jacques Yves; Kimmel, Donald. B.; Leger, Serge; Masse, Frederic; McGrath, Mary E.; McKay, Daniel J.; Percival, M. David; Riendeau, Denis; Rodan, Sevgi B.; Therien, Michel; Truong, Vouy-Linh; Wesolowski, Gregg; Zamboni, Robert; Black, W. Cameron
CORPORATE SOURCE: Merck Frosst Centre for Therapeutic Research, Pointe-Claire-Dorval, QC, H9R 4P8, Can.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(7), 1985-1989
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:403771
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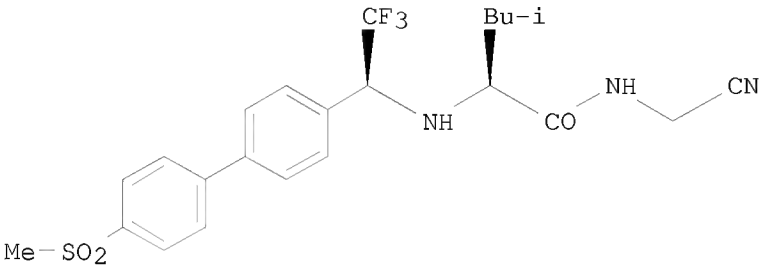


I

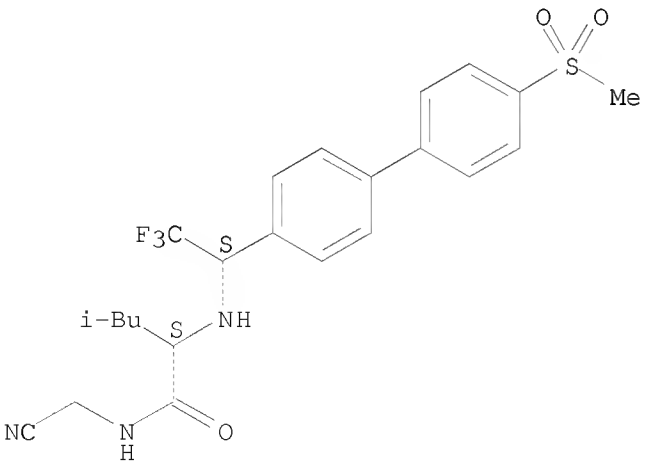
AB Based on our previous study with trifluoroethylamine as a P2-P3 amide isostere of cathepsin K inhibitor, further optimization led to identification of L-873724 (I) as a potent and selective non-basic cathepsin K inhibitor. This compound showed excellent pharmacokinetics and efficacy in an ovariectomized (OVX) rhesus monkey model. The vols. of distribution close to unity were consistent with this compound not being lysosomotropic, which is a characteristic of basic cathepsin K inhibitors.

IT 603139-12-4P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(trifluoromethyl leucine derivs. as cathepsin K inhibitors)

RN 603139-12-4 CAPLUS

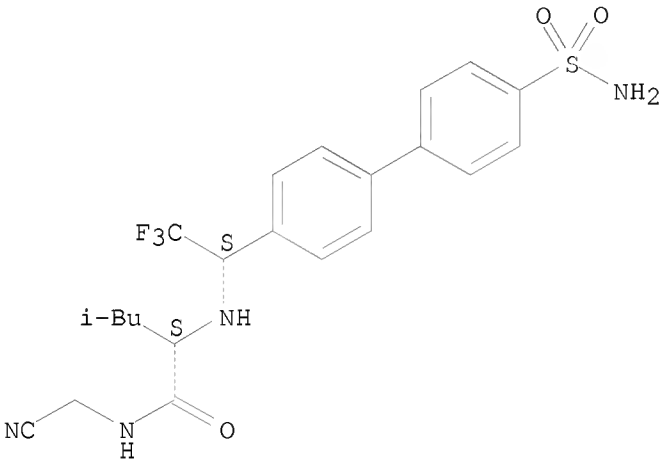
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



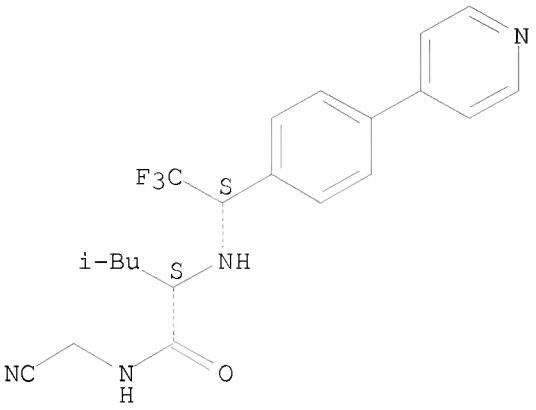
IT 603139-13-5P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(trifluoromethyl leucine derivs. as cathepsin K inhibitors)
RN 603139-13-5 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4'-(aminosulfonyl)[1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



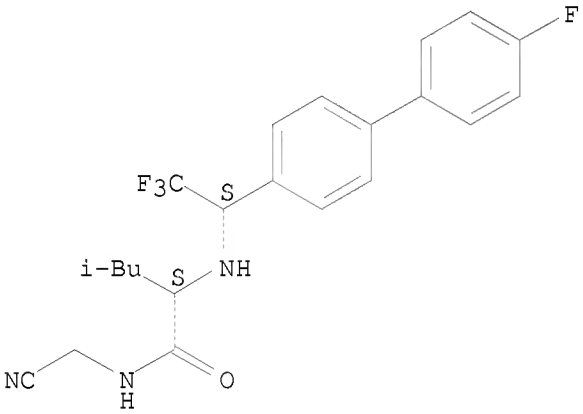
IT 603139-47-5P 603139-54-4P 603139-61-3P
603139-65-7P 603139-66-8P 603139-75-9P
603139-79-3P 603139-87-3P 603139-92-0P
603140-08-5P 603140-40-5P 603140-42-7P
603140-47-2P 603140-50-7P 603140-54-1P
603140-71-2P 603140-81-4P 603140-82-5P
603141-12-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(trifluoromethyl leucine derivs. as cathepsin K inhibitors)
RN 603139-47-5 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(4-pyridinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



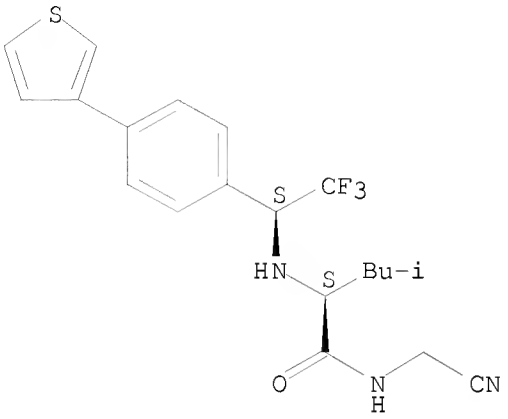
RN 603139-54-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-(4'-fluoro[1,1'-biphenyl]-4-yl)ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



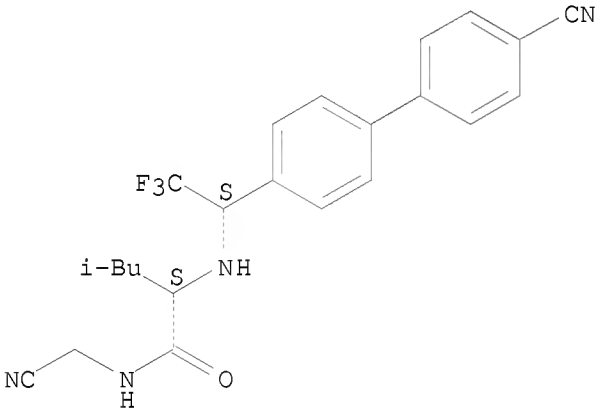
RN 603139-61-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(3-thienyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



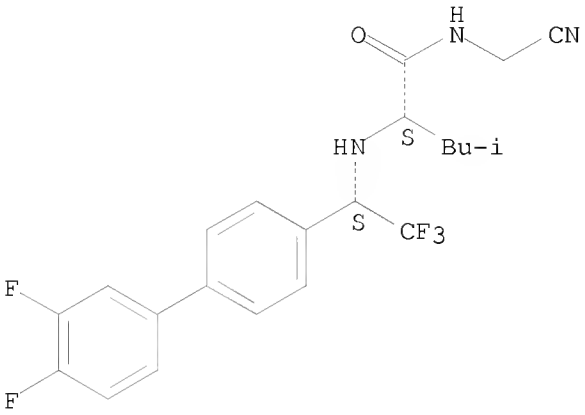
RN 603139-65-7 CAPLUS
CN Pentanamide, 2-[[(1S)-1-(4'-cyano[1,1'-biphenyl]-4-yl)-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



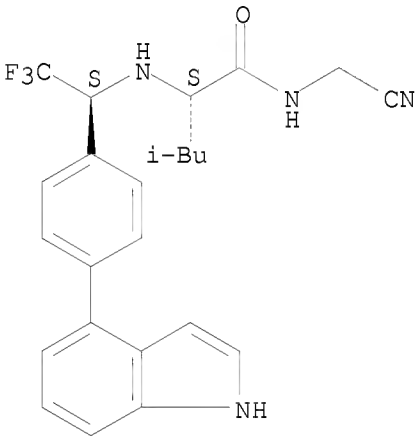
RN 603139-66-8 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[(1S)-1-(3',4'-difluoro[1,1'-biphenyl]-4-yl)-2,2,2-trifluoroethyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



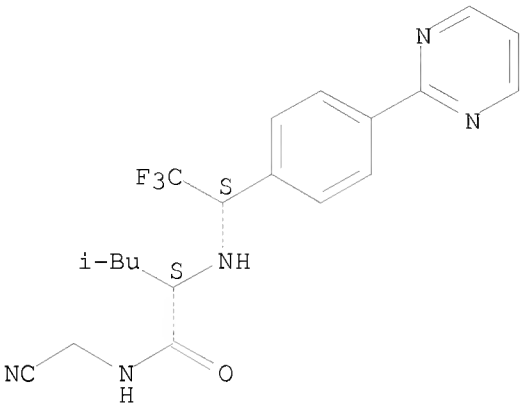
RN 603139-75-9 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(1H-indol-4-yl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



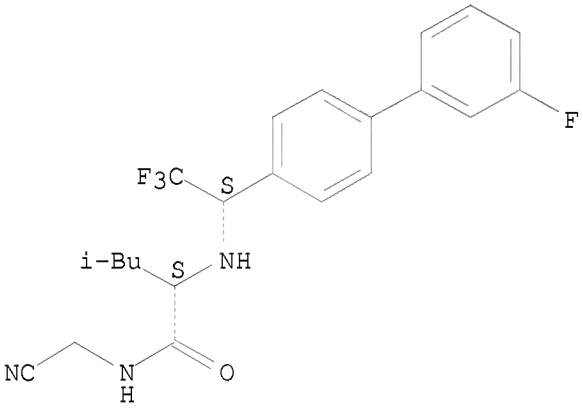
RN 603139-79-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(2-pyrimidinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



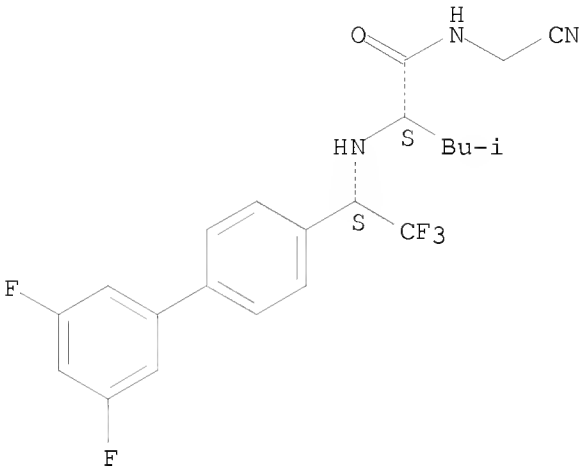
RN 603139-87-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-(3'-fluoro[1,1'-biphenyl]-4-yl)ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



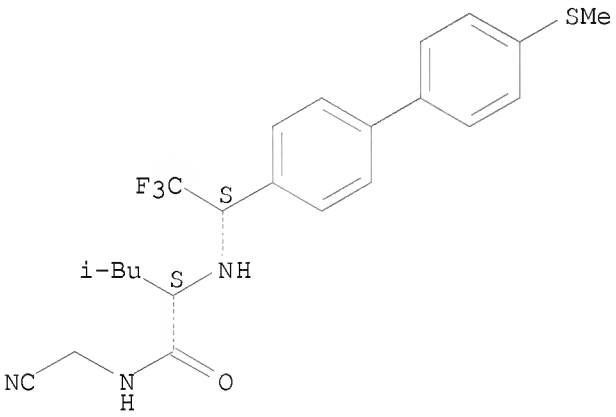
RN 603139-92-0 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[(1S)-1-(3',5'-difluoro[1,1'-biphenyl]-4-yl)-2,2,2-trifluoroethyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



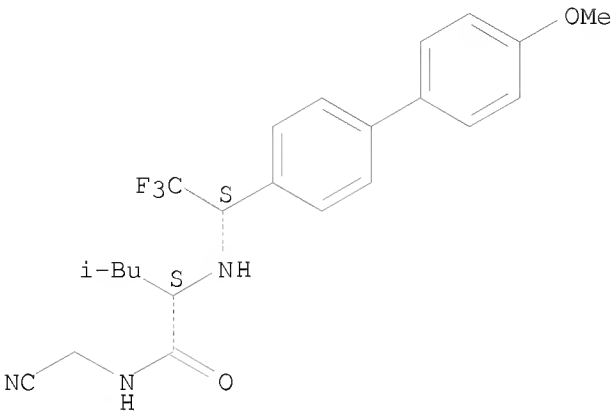
RN 603140-08-5 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylthio)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



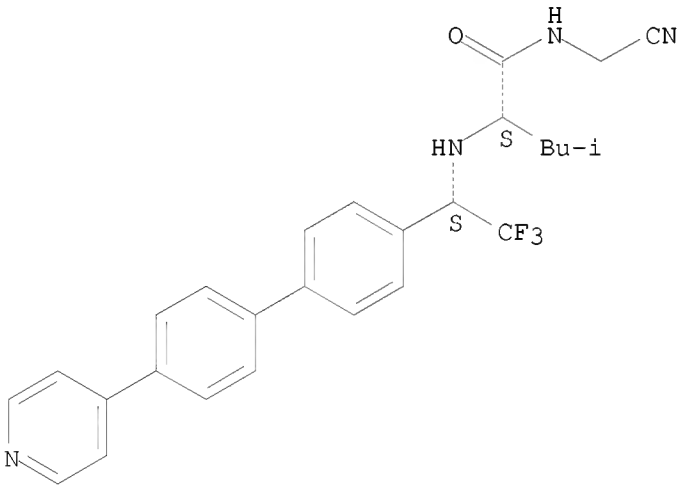
RN 603140-40-5 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-(4'-methoxy[1,1'-biphenyl]-4-yl)ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



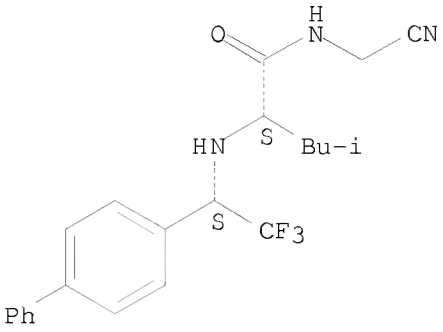
RN 603140-42-7 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(4-pyridinyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



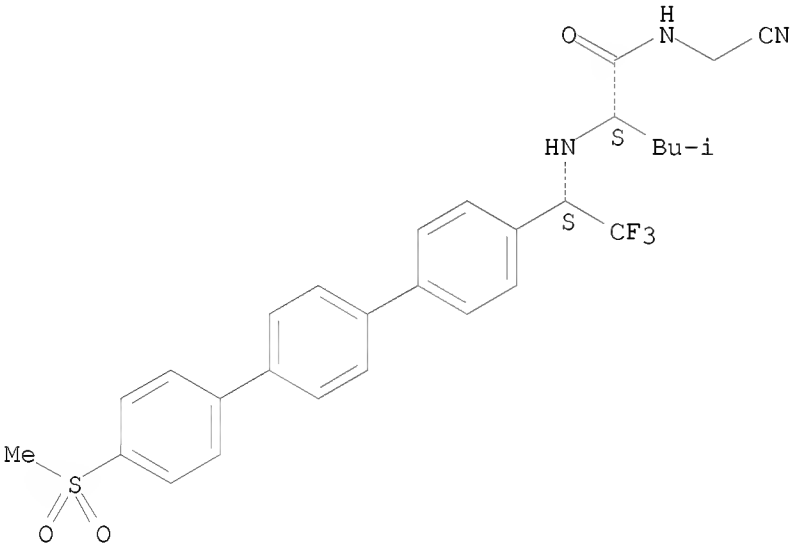
RN 603140-47-2 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[1,1'-biphenyl]-4-yl-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



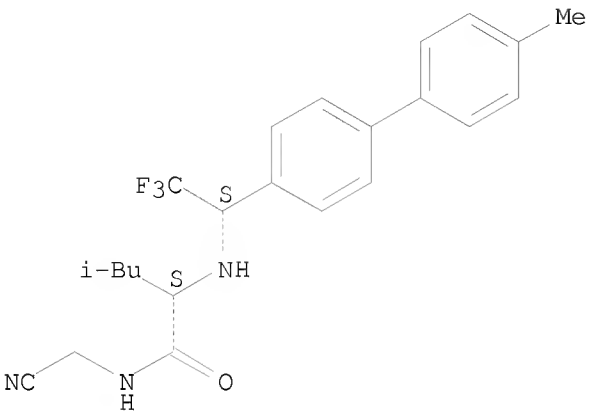
RN 603140-50-7 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4''-(methylsulfonyl)[1,1':4',1''-terphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



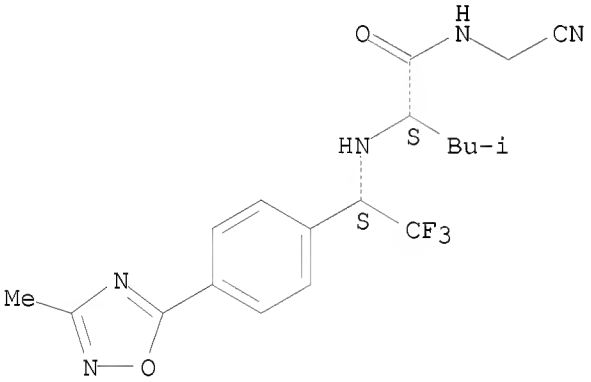
RN 603140-54-1 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-(4'-methyl[1,1'-biphenyl]-4-yl)ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



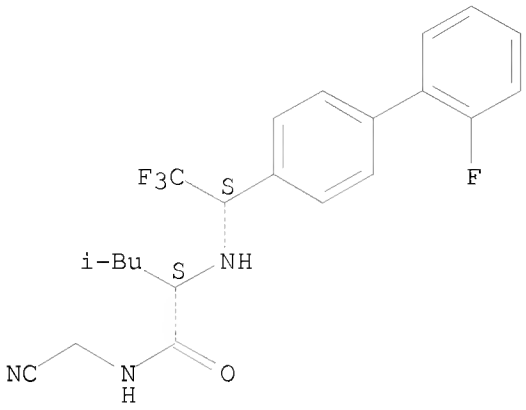
RN 603140-71-2 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



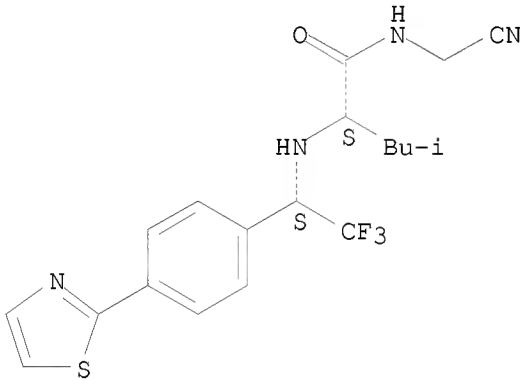
RN 603140-81-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-(2'-fluoro[1,1'-biphenyl]-4-yl)ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



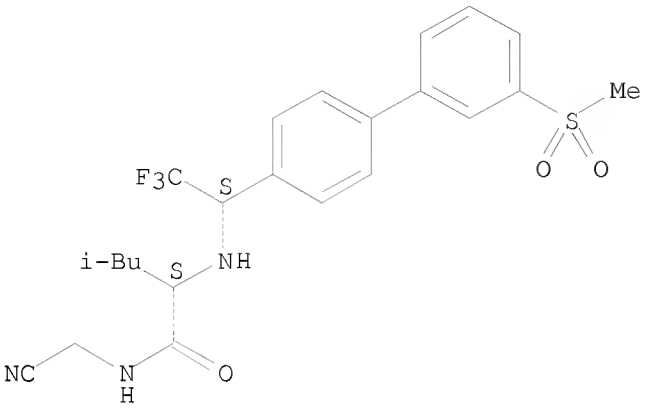
RN 603140-82-5 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(2-thiazolyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



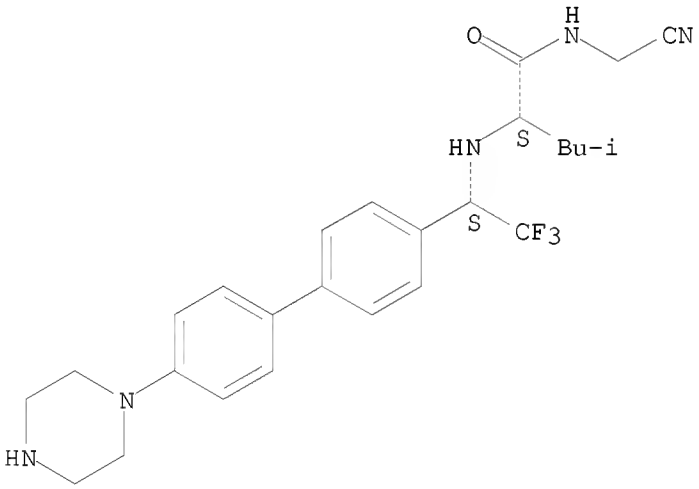
RN 603141-12-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[3'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



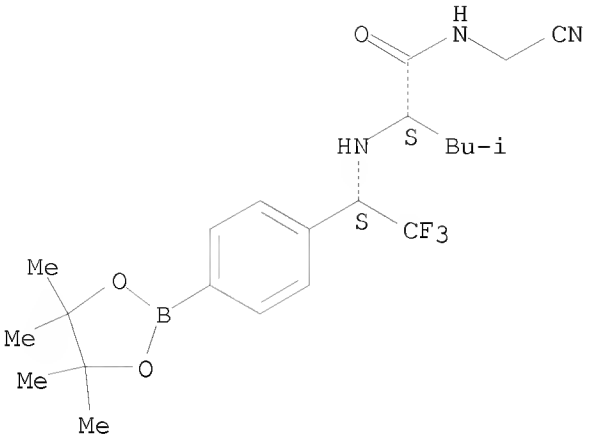
IT 867011-62-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(trifluoromethyl leucine derivs. as cathepsin K inhibitors)
RN 867011-62-9 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(1-piperazinyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 603142-84-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(trifluoromethyl leucine derivs. as cathepsin K inhibitors)
RN 603142-84-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

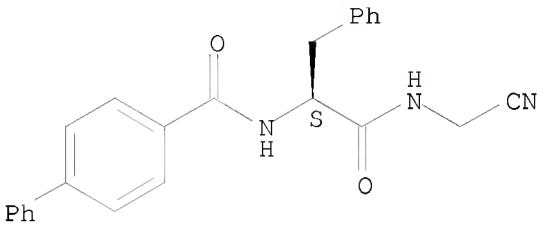
L4 ANSWER 19 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1168545 CAPLUS
DOCUMENT NUMBER: 144:88534
TITLE: Interaction of Papain-like Cysteine Proteases with Dipeptide-Derived Nitriles
AUTHOR(S): Loeser, Reik; Schilling, Klaus; Dimmig, Elke; Guetschow, Michael
CORPORATE SOURCE: Pharmazeutisches Institut, Rheinische Friedrich-Wilhelms-Universitaet Bonn, Bonn, D-53115, Germany
SOURCE: Journal of Medicinal Chemistry (2005), 48(24), 7688-7707
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:88534

AB A series of 44 dipeptide nitriles with various amino acids at the P2 position and glycine nitrile at position P1 were prepared and evaluated as inhibitors of cysteine proteinases. With respect to the important contribution of the P2-S2 interaction to the formation of enzyme-inhibitor complexes, it was focused to introduce structural diversity into the P2 side chain. Nonproteinogenic amino acids were introduced, and systematic fluorine, bromine, and Ph scans for phenylalanine in the P2 position were performed. Moreover, the N-terminal protection was varied. Kinetic investigations were carried out with cathepsin L, S, and K as well as papain. Changes in the backbone structure of the parent N-(tert-butoxycarbonyl)-phenylalanyl-glycine-nitrile (16), such as the introduction of an R-configured amino acid or an azaamino acid into P2 as well as methylation of the P1 nitrogen, resulted in a drastic loss of affinity. Exemplarily, the cyano group of 16 was replaced by an aldehyde or Me ketone function. Structure-activity relationships were discussed with respect to the substrate specificity of the target enzymes.

IT 872217-26-0P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation and biol. activity of dipeptide nitriles as inhibitors of cysteine proteases)
RN 872217-26-0 CAPLUS
CN Benzenepropanamide, α-[([1,1'-biphenyl]-4-ylcarbonyl)amino]-N-(cyanomethyl)-, (αS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1163288 CAPLUS
DOCUMENT NUMBER: 144:546
TITLE: Lysosomotropism of Basic Cathepsin K Inhibitors Contributes to Increased Cellular Potencies against Off-Target Cathepsins and Reduced Functional Selectivity
AUTHOR(S): Falgueyret, Jean-Pierre; Desmarais, Sylvie; Oballa, Renata; Black, W. Cameron; Cromlish, Wanda; Khougaz, Karine; Lamontagne, Sonia; Masse, Frederic; Riendeau, Denis; Toulmond, Sylvie; Percival, M. David
CORPORATE SOURCE: Departments of Biochemistry, Molecular Biology and Pharmacology, Medicinal Chemistry, and Pharmaceutical Research and Development, Merck Frosst Centre for Therapeutic Research, Kirkland, QC, Can.
SOURCE: Journal of Medicinal Chemistry (2005), 48(24), 7535-7543
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 144:546
AB The lysosomal cysteine protease cathepsin K is a target for osteoporosis therapy. The aryl-piperazine-containing cathepsin K inhibitor CRA-013783/L-006235 (1) displays greater than 4000-fold selectivity against the lysosomal/endosomal antitargets cathepsin B, L, and S. However, 1 and other aryl-piperazine-containing analogs, including balicatib (10), are .apprx.10-100-fold more potent in cell-based enzyme occupancy assays than against each purified enzyme. This phenomenon arises from their basic, lipophilic nature, which results in lysosomal trapping. Consistent with its lysosomotropic nature, 1 accumulates in cells and in rat tissues of high lysosome content. In contrast, nonbasic aryl-morpholino-containing analogs do not exhibit lysosomotropic properties. Increased off-target activities of basic cathepsin K inhibitors were observed in a cell-based cathepsin S antigen presentation assay. No potency increases of basic inhibitors in a functional cathepsin K bone resorption

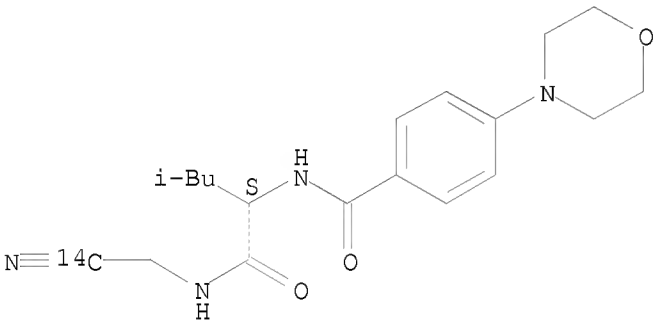
whole cell assay were detected. Therefore, basic cathepsin K inhibitors, such as 1, suffer from reduced functional selectivities compared to those predicted using purified enzyme assays.

IT 870100-90-6P
RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(piperazine and morpholino-containing cathepsin K inhibitors preparation, lysosomotropic and cathepsins B,K,L, and S inhibiting properties)

RN 870100-90-6 CAPLUS

CN Benzamide, N-[(1S)-1-[[(cyano-14C-methyl)amino]carbonyl]-3-methylbutyl]-4-(4-morpholinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1123751 CAPLUS
DOCUMENT NUMBER: 143:399840
TITLE: Cathepsin B inhibitors for the treatment of diabetes and metabolic syndrome
INVENTOR(S): Broder, Samuel E.; Rydzewski, Robert M.
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005097103	A2	20051020	WO 2005-US11065	20050401
WO 2005097103	A3	20060810		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,

RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-558933P P 20040401

OTHER SOURCE(S): MARPAT 143:399840

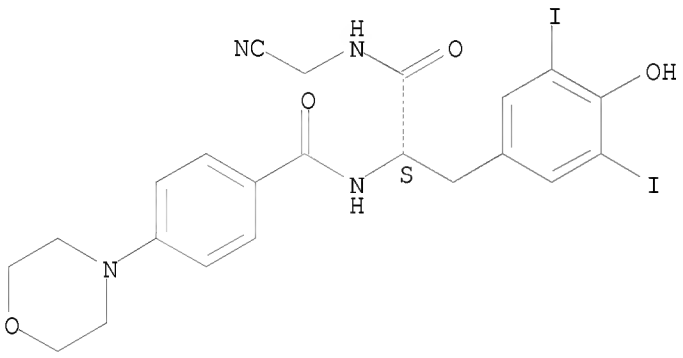
AB The invention is directed to the treatment of e.g. Type II diabetes by administering a cathepsin B inhibitor(s).

IT 676477-45-5 676477-47-7 676477-53-5
676477-54-6 676477-55-7 676477-63-7
867030-89-5 867031-00-3 867031-02-5
867031-03-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cathepsin B inhibitors for treatment of diabetes and metabolic syndrome)

RN 676477-45-5 CAPLUS

CN Benzenepropanamide, N-(cyanomethyl)-4-hydroxy-3,5-diiodo-α-[[4-(4-morpholinyl)benzoyl]amino]-, (αS)- (CA INDEX NAME)

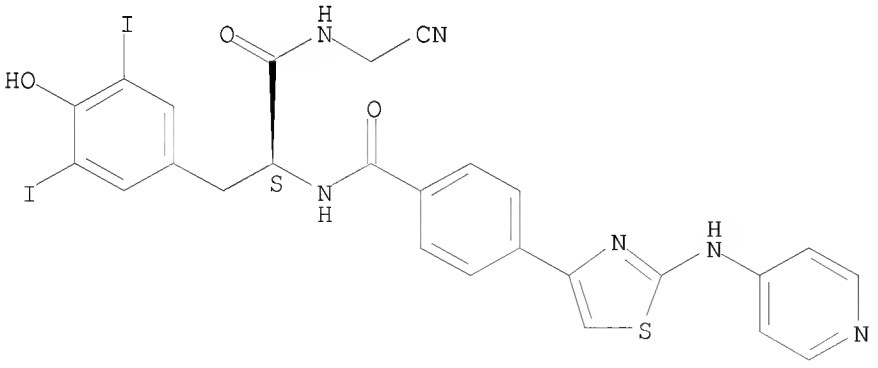
Absolute stereochemistry.



RN 676477-47-7 CAPLUS

CN Benzenepropanamide, N-(cyanomethyl)-4-hydroxy-3,5-diiodo-α-[[4-[2-(4-pyridinylamino)-4-thiazolyl]benzoyl]amino]-, (αS)- (CA INDEX NAME)

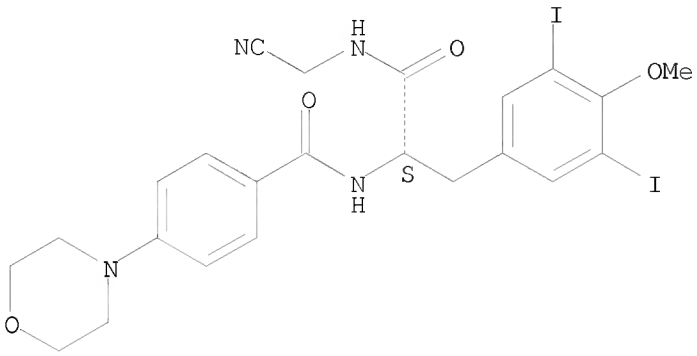
Absolute stereochemistry.



RN 676477-53-5 CAPLUS

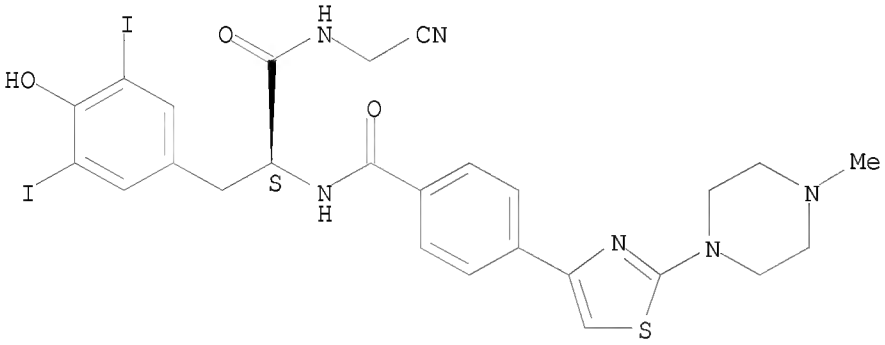
CN Benzenepropanamide, N-(cyanomethyl)-3,5-diiodo-4-methoxy-α-[[4-(4-morpholinyl)benzoyl]amino]-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.



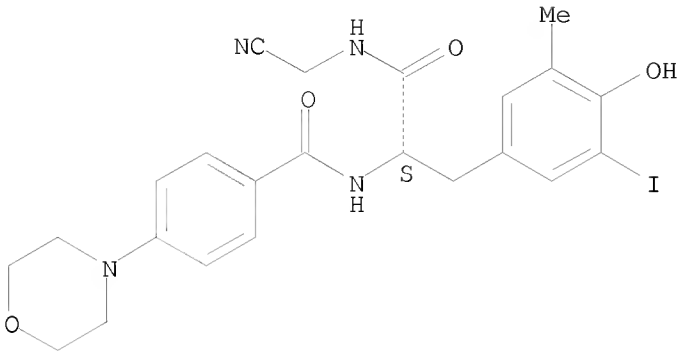
RN 676477-54-6 CAPLUS
CN Benzenepropanamide, N-(cyanomethyl)-4-hydroxy-3,5-diiodo-α-[[4-[2-(4-methyl-1-piperazinyl)-4-thiazolyl]benzoyl]amino]-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.



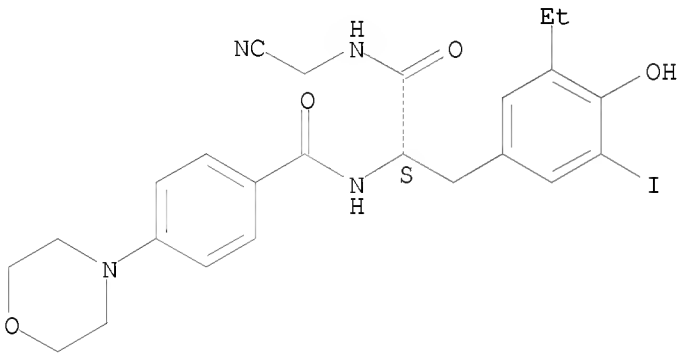
RN 676477-55-7 CAPLUS
CN Benzenepropanamide, N-(cyanomethyl)-4-hydroxy-3-iodo-5-methyl-α-[[4-(4-morpholinyl)benzoyl]amino]-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.



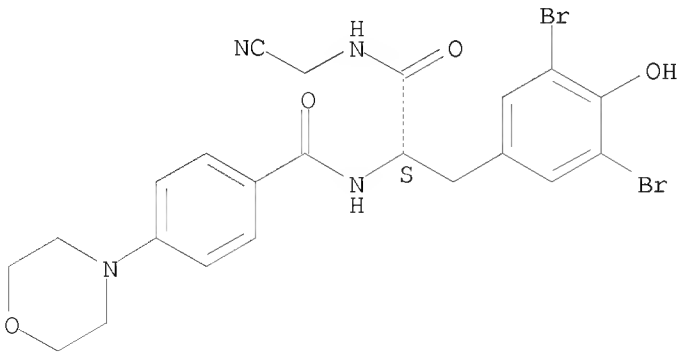
RN 676477-63-7 CAPLUS
CN Benzenepropanamide, N-(cyanomethyl)-3-ethyl-4-hydroxy-5-iodo-α-[[4-(4-morpholinyl)benzoyl]amino]-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.



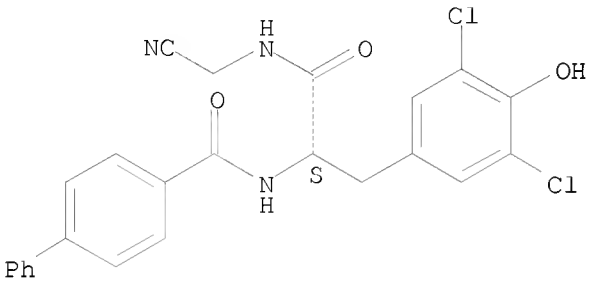
RN 867030-89-5 CAPLUS
CN Benzenepropanamide, 3,5-dibromo-N-(cyanomethyl)-4-hydroxy-α-[[4-(4-morpholinyl)benzoyl]amino]-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.



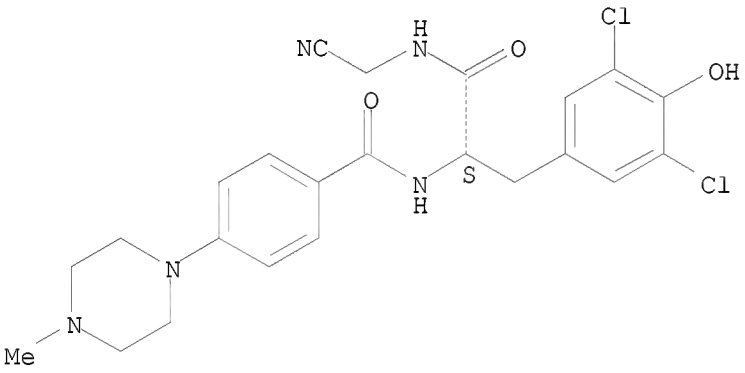
RN 867031-00-3 CAPLUS
CN Benzenepropanamide, α-[([1,1'-biphenyl]-4-ylcarbonyl)amino]-3,5-dichloro-N-(cyanomethyl)-4-hydroxy-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.



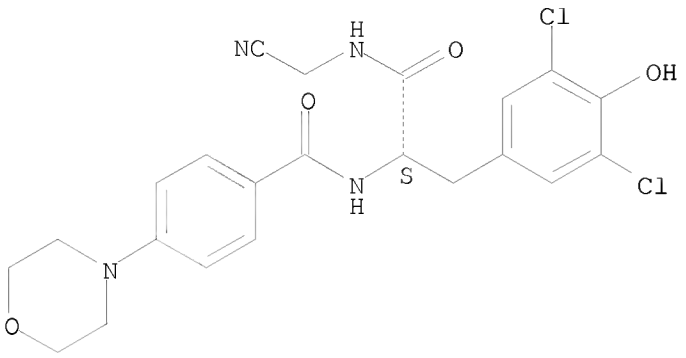
RN 867031-02-5 CAPLUS
CN Benzenepropanamide, 3,5-dichloro-N-(cyanomethyl)-4-hydroxy-α-[[4-(4-methyl-1-piperazinyl)benzoyl]amino]-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.

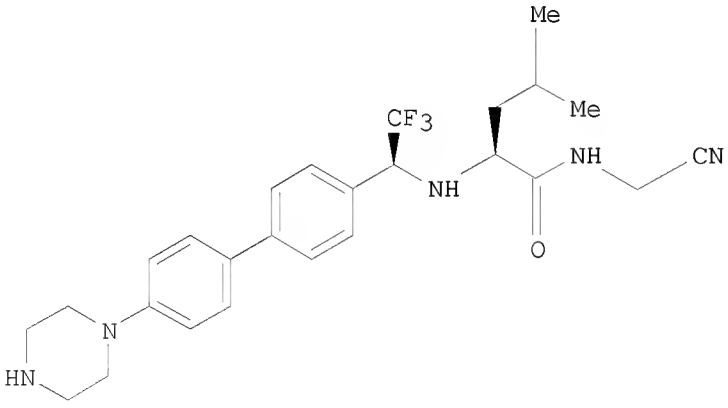


RN 867031-03-6 CAPLUS
CN Benzenepropanamide, 3,5-dichloro-N-(cyanomethyl)-4-hydroxy-α-[[4-(4-morpholinyl)benzoyl]amino]-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 22 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1024918 CAPLUS
DOCUMENT NUMBER: 143:398880
TITLE: Trifluoroethylamines as amide isosteres in inhibitors of cathepsin K
AUTHOR(S): Black, W. Cameron; Bayly, Christopher I.; Davis, Dana E.; Desmarais, Sylvie; Falgueyret, Jean-Pierre; Leger, Serge; Li, Chun Sing; Masse, Frederic; McKay, Daniel J.; Palmer, James T.; Percival, M. David; Robichaud, Joel; Tsou, Nancy; Zamboni, Robert
CORPORATE SOURCE: Merck Frosst Centre for Therapeutic Research, Pointe-Claire-Dorval, QC, H9R 4P8, Can.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(21), 4741-4744
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:398880
GI



I

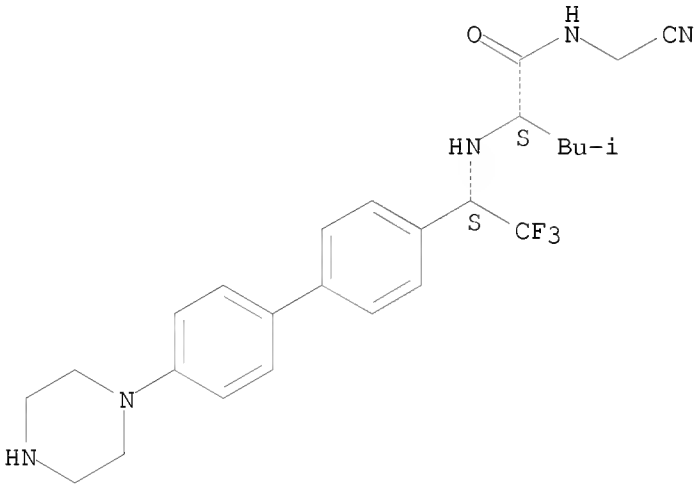
AB The P2-P3 amide of dipeptide cathepsin K inhibitors can be replaced by the

metabolically stable trifluoroethylamine group. The nonbasic nature of the nitrogen allows the important hydrogen bond to Gly66 to be made. The resulting compds. are 10- to 20-fold more potent than the corresponding amide derivs. Compound (I) is a 5 pM inhibitor of human cathepsin K with >10,000-fold selectivity over other cathepsins.

IT 867011-62-9P 867011-63-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(trifluoroethylamines as amide isosteres in inhibitors of cathepsin K)

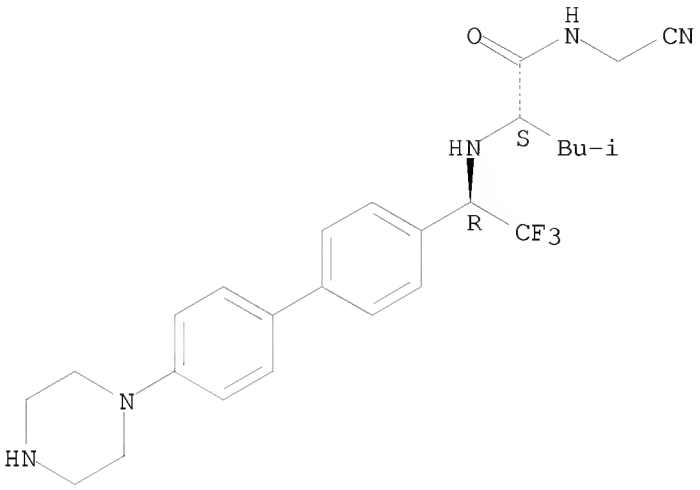
RN 867011-62-9 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(1-piperazinyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 867011-63-0 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1R)-2,2,2-trifluoro-1-[4'-(1-piperazinyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

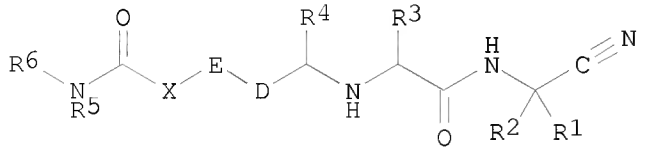
L4 ANSWER 23 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:547595 CAPLUS
DOCUMENT NUMBER: 143:60251
TITLE: Preparation of peptide nitriles as cathepsin cysteine protease inhibitors
INVENTOR(S): Boyd, Michael; Lau, Cheuk; Mellon, Christophe; Roy, Bruno; Scheigetz, John; Truong, Vouy Linh
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005056529	A1	20050623	WO 2004-CA2101	20041209
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004296905	A1	20050623	AU 2004-296905	20041209
CA 2548600	A1	20050623	CA 2004-2548600	20041209
EP 1694647	A1	20060830	EP 2004-802278	20041209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				

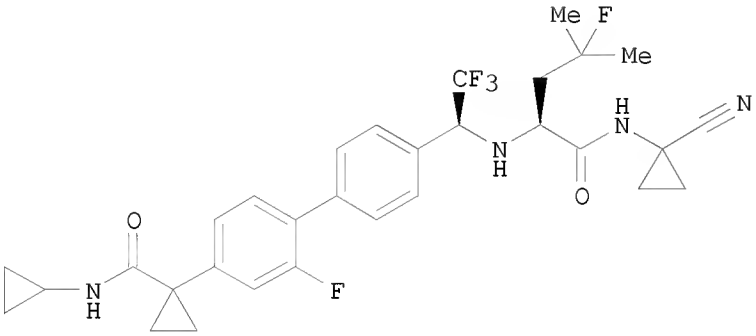
CN 1906164	A	20070131	CN 2004-80036642		20041209
JP 2007513890	T	20070531	JP 2006-543331		20041209
IN 2006DN03000	A	20070803	IN 2006-DN3000		20060525
US 20070099893	A1	20070503	US 2006-581692		20060606
PRIORITY APPLN. INFO.:			US 2003-529254P	P	20031212
			WO 2004-CA2101	W	20041209

OTHER SOURCE(S): CASREACT 143:60251; MARPAT 143:60251

GI



I



II

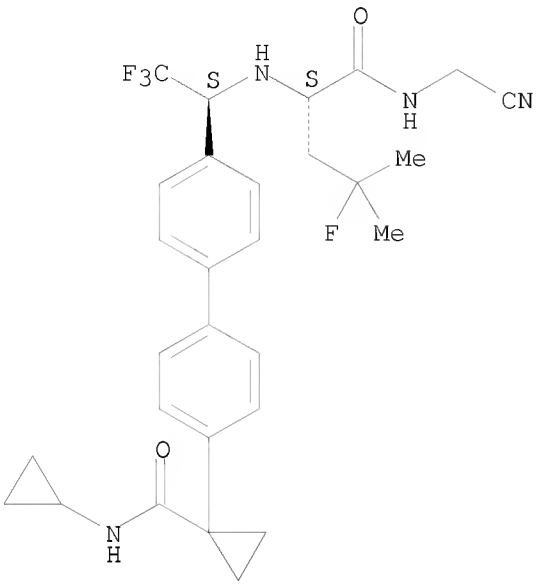
AB The invention relates to a novel class of compds. I [R1, R2 are independently H, (un)substituted alkyl, alkenyl, aryl, heteroaryl or heterocyclyl; or R1R2C form a cycloalkyl or heterocyclyl ring; R3 is (un)substituted alkyl or alkenyl; R4 is alkyl or haloalkyl; R5 is H or alkyl; D, E are independently (un)substituted aryl or heteroaryl; X is cycloalkyl or CRaRb, where Ra, Rb are H or alkyl optionally substituted by OR5] which are cysteine protease inhibitors (e.g., inhibitors of cathepsins K, L, S and B) and are useful for treating osteoporosis and other diseases in which inhibition of bone resorption is indicated. Thus, 4-fluoro-L-leucine 1-cyanocyclopropylamide II was prepared via coupling of intermediates 1-(4-bromo-3-fluorophenyl)-N-cyclopropylcyclopropanecarboxamide with N1-(1-cyanocyclopropyl)-4-fluoro-N2-[(1S)-2,2,2-trifluoro-1-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]ethyl]-L-leucinamide in the presence of [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II).

IT 854268-13-6P 854268-19-2P 854268-47-6P
854268-48-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptide nitriles as cathepsin cysteine protease inhibitors)

RN 854268-13-6 CAPLUS

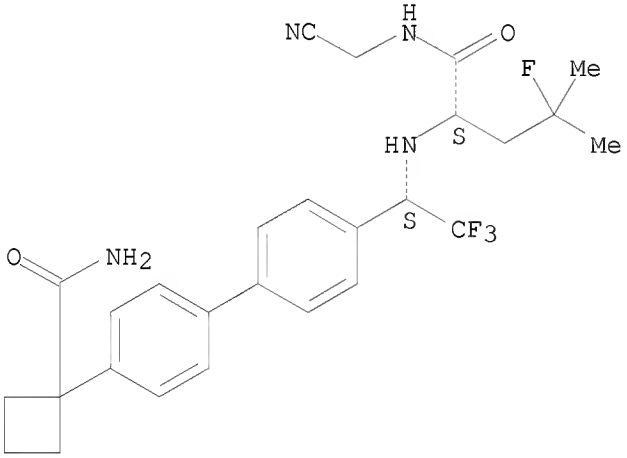
CN Cyclopropanecarboxamide, 1-[4'-[(1S)-1-[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-fluoro-3-methylbutyl]amino]-2,2,2-trifluoroethyl][1,1'-biphenyl]-4-yl]-N-cyclopropyl- (CA INDEX NAME)

Absolute stereochemistry.



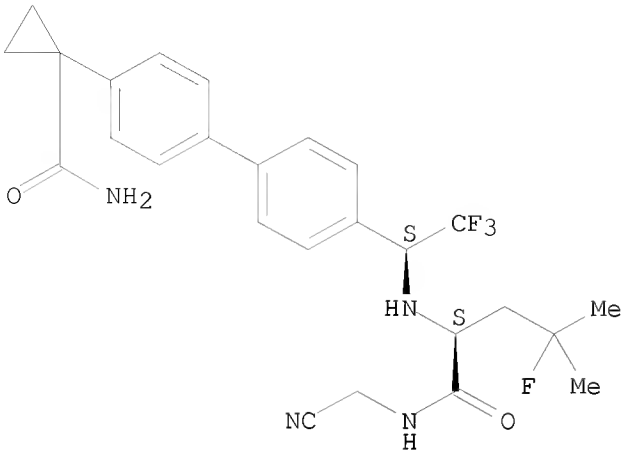
RN 854268-19-2 CAPLUS
CN Cyclobutanecarboxamide, 1-[4'-[(1S)-1-[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-fluoro-3-methylbutyl]amino]-2,2,2-trifluoroethyl][1,1'-biphenyl]-4-yl]- (CA INDEX NAME)

Absolute stereochemistry.



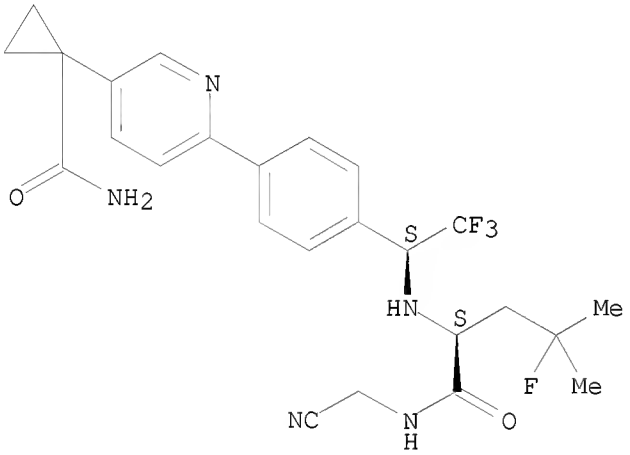
RN 854268-47-6 CAPLUS
CN Cyclopropanecarboxamide, 1-[4'-[(1S)-1-[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-fluoro-3-methylbutyl]amino]-2,2,2-trifluoroethyl][1,1'-biphenyl]-4-yl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 854268-48-7 CAPLUS
CN Cyclopropanecarboxamide, 1-[6-[4-[(1S)-1-[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-fluoro-3-methylbutyl]amino]-2,2,2-trifluoroethyl]phenyl]-3-pyridinyl]- (CA INDEX NAME)

Absolute stereochemistry.



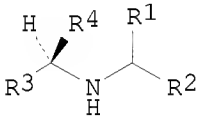
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:219775 CAPLUS
DOCUMENT NUMBER: 142:280425
TITLE: Preparation of amino acid derivatives as cathepsin inhibitors
INVENTOR(S): Bayly, Christopher; Black, Cameron; McKay, Daniel J.
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005021487	A1	20050310	WO 2004-CA1577	20040823
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004268707	A1	20050310	AU 2004-268707	20040823
CA 2535366	A1	20050310	CA 2004-2535366	20040823
EP 1660436	A1	20060531	EP 2004-761741	20040823
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1842515	A	20061004	CN 2004-80024520	20040823
JP 2007503401	T	20070222	JP 2006-524194	20040823
US 20060287402	A1	20061221	US 2006-569351	20060222
IN 2006DN01174	A	20071012	IN 2006-DN1174	20060306
PRIORITY APPLN. INFO.:			US 2003-498017P P	20030827
			WO 2004-CA1577 W	20040823

OTHER SOURCE(S): CASREACT 142:280425; MARPAT 142:280425
GI



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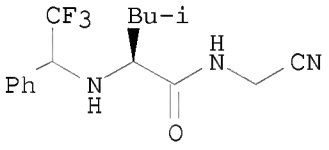


II

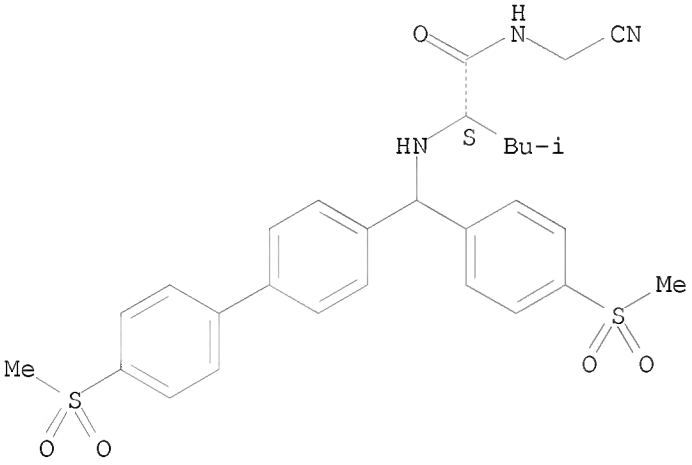
AB The invention relates to compds. I which are cysteine protease inhibitors, including but not limited to inhibitors of cathepsins K, L, S and B, and are useful for treating diseases in which inhibition of bone resorption is indicated, e.g., osteoporosis, osteoarthritis and rheumatoid arthritis. Thus, a mixture of L-leucine Me ester hydrochloride, 2,2,2-trifluoroacetophenone, diisopropylethylamine and TiCl4 in CH2Cl2 was stirred overnight, addnl. TiCl4 added, and the mixture stirred an addnl. 3 h. A solution of NaCNBH3 in MeOH was added and the mixture stirred 2 h to afford Me N-(2,2,2-trifluoro-1-phenylethyl)-L-leucinate. Saponification of the ester and reaction with aminoacetonitrile hydrochloride in DMF in the presence of PyBOP and Et3N yielded L-leucinamide derivative II.

IT 603139-08-8P 603139-12-4P 603140-63-2P
603141-70-4P 603142-15-0P 847361-50-6P
847361-57-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid derivs. as cathepsin inhibitors)

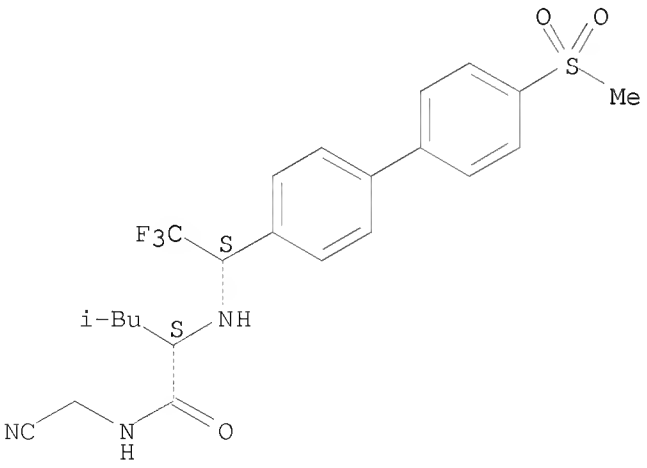
RN 603139-08-8 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl][4-(methylsulfonyl)phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



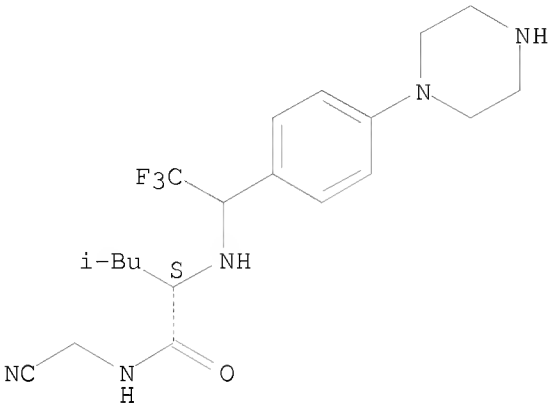
RN 603139-12-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



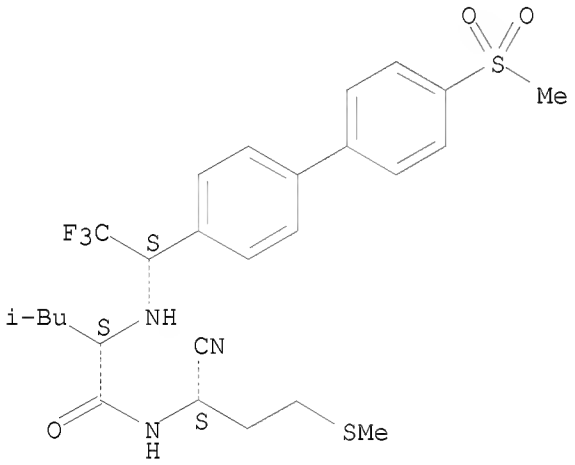
RN 603140-63-2 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4-(1-piperazinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



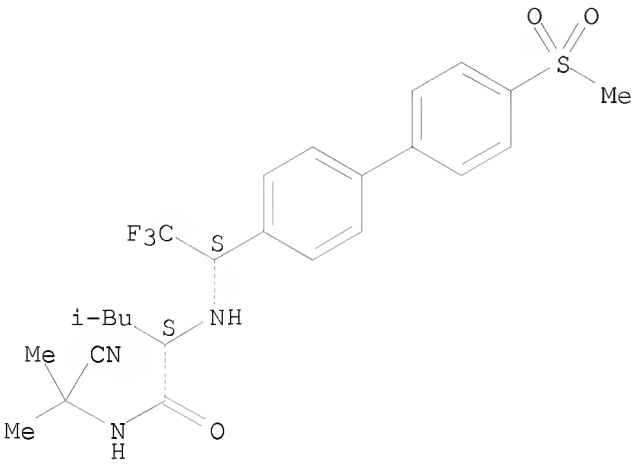
RN 603141-70-4 CAPLUS
CN Pentanamide, N-[(1S)-1-cyano-3-(methylthio)propyl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



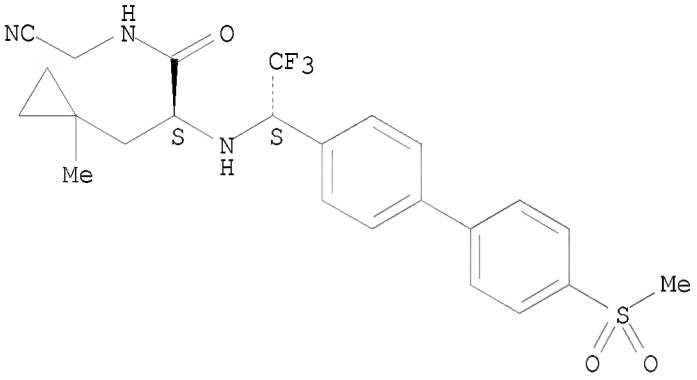
RN 603142-15-0 CAPLUS
CN Pentanamide, N-(1-cyano-1-methylethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



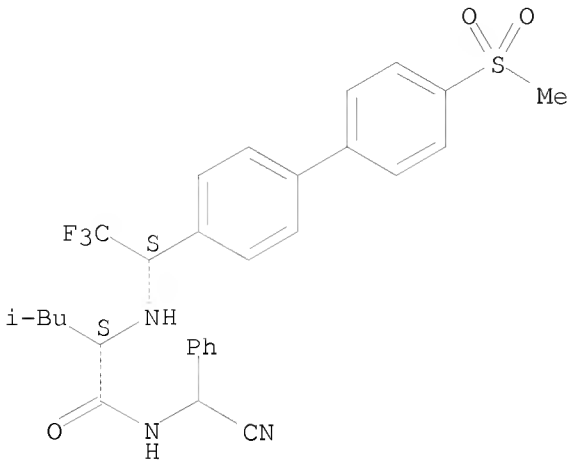
RN 847361-50-6 CAPLUS
CN Cyclopropanepropanamide, N-(cyanomethyl)-1-methyl-α-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.



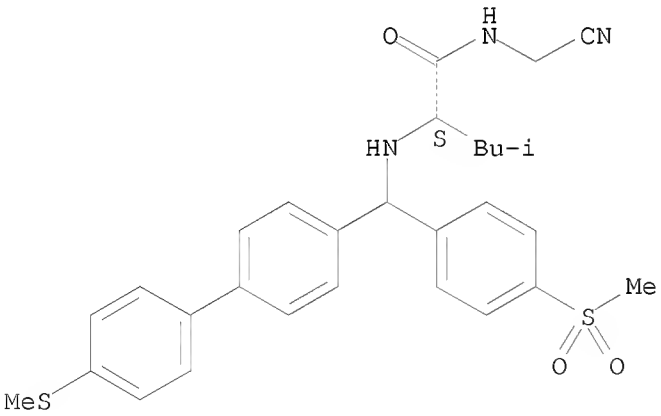
RN 847361-57-3 CAPLUS
CN Pentanamide, N-(cyanophenylmethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



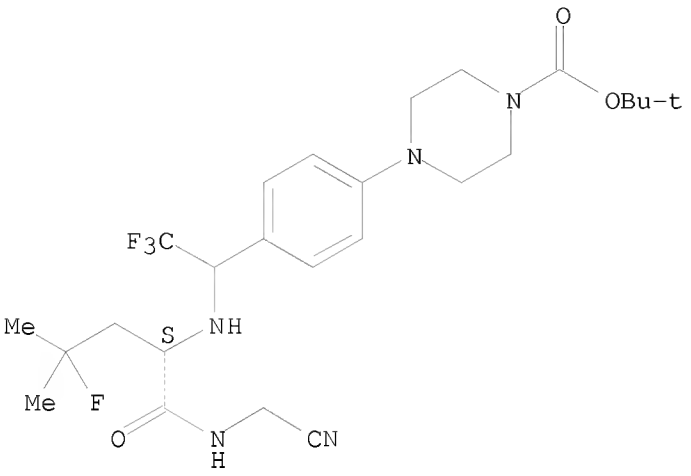
IT 603141-16-8P 847361-66-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of amino acid derivs. as cathepsin inhibitors)
RN 603141-16-8 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[[4-(methylsulfonyl)phenyl][4'-(methylthio)[1,1'-biphenyl]-4-yl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 847361-66-4 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-[1-[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-fluoro-3-methylbutyl]amino]-2,2,2-trifluoroethyl]phenyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:182615 CAPLUS
DOCUMENT NUMBER: 142:280422
TITLE: Preparation of amino acid derivatives as cathepsin cysteine protease inhibitors
INVENTOR(S): Gauthier, Jacques Yves; Truong, Vouy Linh
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005019161	A1	20050303	WO 2004-CA1524	20040819
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004266740	A1	20050303	AU 2004-266740	20040819
CA 2535359	A1	20050303	CA 2004-2535359	20040819
EP 1673336	A1	20060628	EP 2004-761688	20040819
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1839114	A	20060927	CN 2004-80023760	20040819

JP 2007502781	T	20070215	JP 2006-523498		20040819
US 20060287373	A1	20061221	US 2006-568495		20060215
US 7312353	B2	20071225			
IN 2006DN01177	A	20071012	IN 2006-DN1177		20060306
PRIORITY APPLN. INFO.:			US 2003-496825P	P	20030821
			WO 2004-CA1524	W	20040819

OTHER SOURCE(S): CASREACT 142:280422; MARPAT 142:280422

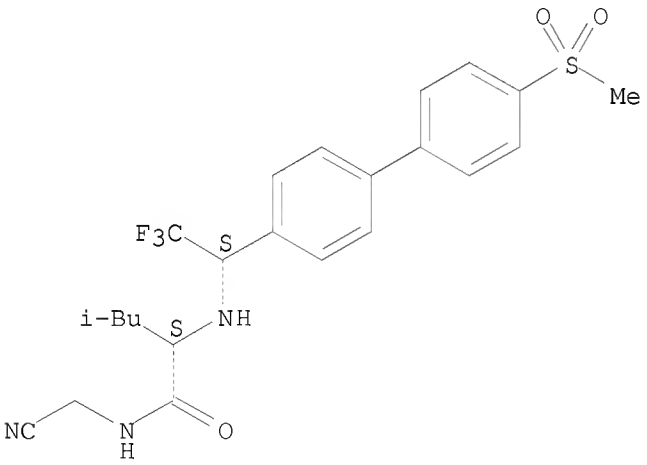
AB The invention relates to amino acid derivs. HO2C-Gn-E-D-CHR4NHCHR3CONHCR1R2CN [R1, R2, R3 are independently H, (un)substituted alkyl or alkenyl; R4 is H or haloalkyl; D, E are independently (un)substituted aryl or heteroaryl; G is (un)substituted alkyl, alkoxy, aryl, heteroaryl, cycloalkyl, heterocyclyl, O, imino, S, SO, SO2 or CO; n is 1-3], which are cysteine protease inhibitors and are useful for treating diseases in which inhibition of bone resorption is indicated, e.g., osteoporosis. Thus, (S)-p-MeSO2C6H4C6H4-p-CH(CF3)-L-Leu-NHCH2CN was prepared by a multistep sequence in which the reactants are L-leucinol, trifluoroacetaldehyde Me hemiacetal, 1,4-dibromobenzene, 4-(methylthio)phenylboronic acid, and aminoacetonitrile hydrochloride.

IT 603139-12-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid derivs. as cathepsin cysteine protease inhibitors)

RN 603139-12-4 CAPLUS

CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 26 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:610055 CAPLUS

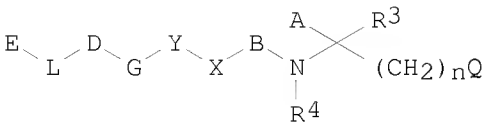
DOCUMENT NUMBER: 141:157473

TITLE: Preparation of amino acid derivatives as antibacterial agents

INVENTOR(S): Anderson, Neils H.; Bowman, Jason; Erwin, Alice; Harwood, Eric; Kline, Toni; Mdluli, Khisimuzi; Ng, Simon; Pfister, Keith B.; Shawar, Ribhi; Wagman, Allan; Yabannavar, Asha
PATENT ASSIGNEE(S): Chiron Corporation, USA
SOURCE: PCT Int. Appl., 324 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004062601	A2	20040729	WO 2004-US433	20040108
WO 2004062601	A3	20050421		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ				
AU 2004204760	A1	20040729	AU 2004-204760	20040108
CA 2512582	A1	20040729	CA 2004-2512582	20040108
US 20040229955	A1	20041118	US 2004-754928	20040108
EP 1618087	A2	20060125	EP 2004-700887	20040108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1777577	A	20060524	CN 2004-80005935	20040108
JP 2006519772	T	20060831	JP 2006-500858	20040108
MX 2005PA07394	A	20050912	MX 2005-PA7394	20050707
IN 2005KN01343	A	20060915	IN 2005-KN1343	20050712
US 20060154988	A1	20060713	US 2005-187708	20050722
US 7358359	B2	20080415		
US 20070244197	A1	20071018	US 2006-417346	20060503
US 20080269221	A1	20081030	US 2007-837327	20070810
PRIORITY APPLN. INFO.:			US 2003-438523P P	20030108
			US 2003-466974P P	20030430
			US 2003-520211P P	20031113
			US 2004-754928 A1	20040108
			WO 2004-US433 W	20040108

OTHER SOURCE(S): MARPAT 141:157473
GI



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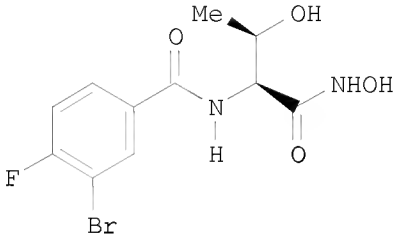


II

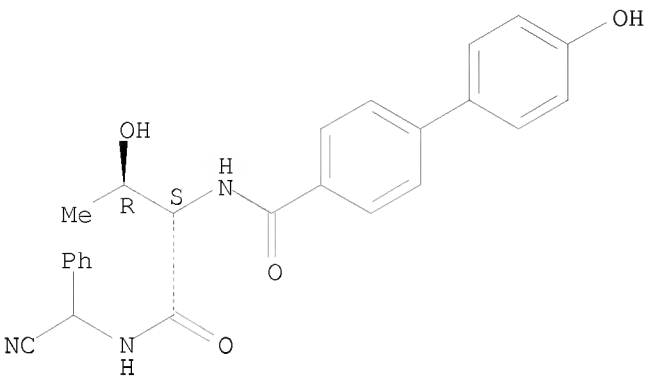
AB Title compds. I [E = absent or H, (un)substituted-alkyl, -alkenyl, -aryl, etc.; L = absent or CONH, NHCO, (un)substituted alkyl, etc.; D = absent or (un)substituted-cycloalkyl, -aryl, -heterocyclyl or -heteroaryl; G = absent or alkene, alkyne, CO, etc.; Y = (un)substituted-cycloalkyl, -aryl, -heterocyclyl or -heteroaryl; X = CO, alkylcarbonyl, alkenylcarbonyl, alkynylcarbonyl, methylene, or when B is absent X and A together form heterocyclic ring; B = absent or substituted aminoalkylcarbonyl; R3 = H or (un)substituted alkyl, or R3 and A together form a cycloalkyl or heterocyclic ring; R4 = H or (un)substituted alkyl, or R4 and A together form a heterocyclic ring; n = 0-2; A = H, acetylene, alkyl, etc.; Q = absent or substituted amide, SH, SO2NH2, CO2H, etc.] are disclosed: As well as stereoisomers, pharmaceutically acceptable salts, esters, and prodrugs thereof; pharmaceutical compns. comprising such compds.; methods of treating bacterial infections by the administration of such compds.; and processes for the preparation of the compds. Thus, e.g., II was prepared via amidation of 3-bromo-4-fluorobenzoic acid with L-threonine Me ester hydrochloride followed by substitution with hydroxylamine hydrochloride. This invention pertains generally to treating infections caused by gram-neg. bacteria. More specifically, the invention described pertains to treating gram-neg. infections by inhibiting activity of UDP-3-O-(R-3-hydroxydecanoyl)-N-acetylglucosamine deacetylase (LpxC). Many of I displayed an IC50 value of less than 10 μM with respect to inhibition of LpxC.

IT 728867-68-3P 728867-70-7P 728867-71-8P
728867-72-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of amino acid derivs. as antibacterial agents)

RN 728867-68-3 CAPLUS

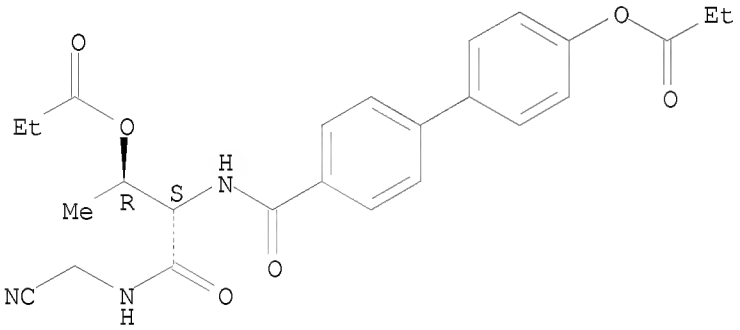
CN [1,1'-Biphenyl]-4-carboxamide, N-[(1S,2R)-1-[[(cyanophenylmethyl)amino]carbonyl]-2-hydroxypropyl]-4'-hydroxy- (CA INDEX NAME)

Absolute stereochemistry.



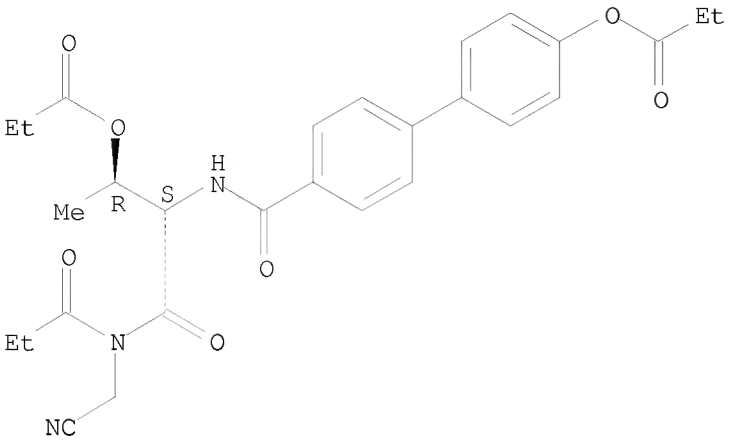
RN 728867-70-7 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[(1S,2R)-1-[[(cyanomethyl)amino]carbonyl]-2-(1-oxopropoxy)propyl]-4'-(1-oxopropoxy)- (CA INDEX NAME)

Absolute stereochemistry.



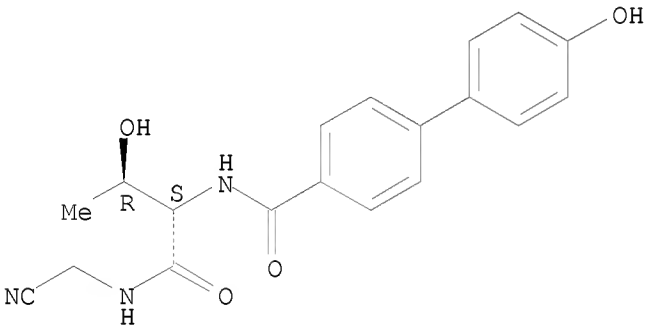
RN 728867-71-8 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[(1S,2R)-1-[[(cyanomethyl)(1-oxopropyl)amino]carbonyl]-2-(1-oxopropoxy)propyl]-4'-(1-oxopropoxy)- (CA INDEX NAME)

Absolute stereochemistry.



RN 728867-72-9 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[(1S,2R)-1-[[(cyanomethyl)amino]carbonyl]-2-hydroxypropyl]-4'-hydroxy- (CA INDEX NAME)

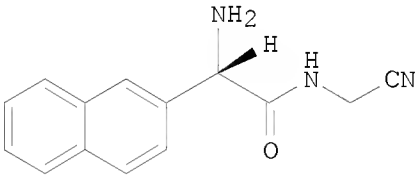
Absolute stereochemistry.



L4 ANSWER 27 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:525097 CAPLUS
DOCUMENT NUMBER: 141:89364
TITLE: Preparation of amino acid cyanoalkylamides as rotamase inhibitors
INVENTOR(S): Knolle, Jochen; Schutkowski, Mike; Hummel, Gerd; Tradler, Thomas; Jobron, Laurence; Christner, Claudia; Stragies, Roland
PATENT ASSIGNEE(S): Jerini A.-G., Germany
SOURCE: Eur. Pat. Appl., 131 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 1433779 A1 20040630 EP 2002-28801 20021223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
WO 2004056755 A2 20040708 WO 2003-EP14838 20031223
WO 2004056755 A3 20040910
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2003300551 A1 20040714 AU 2003-300551 20031223
PRIORITY APPLN. INFO.: EP 2002-28801 A 20021223
WO 2003-EP14838 W 20031223
OTHER SOURCE(S): MARPAT 141:89364
GI



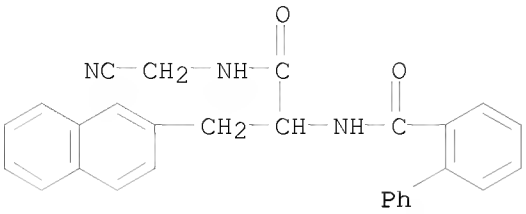
II

AB Title compds. A-B-C-D [A = carboxamido, carboxamic acid ester, etc.; B = absent, alkylcarbonylamino, etc.; C = substituted alkyl; D = alkylalc., alkylnitrile, alkylhydrazide, etc.; I] are prepared For instance, (S)-2-[N-(tert-butoxycarbonyl)amino]-2-(naphthalen-2-yl)acetic acid is coupled to 3-aminoacetonitrile (DMF, HBTu, Et3N) and the resulting amide deprotected (CH2Cl2, TFA) to give II. Example compds. were tested for activity with several rotamases. Compds. I are useful for the treatment of inflammatory and proliferative disorders.

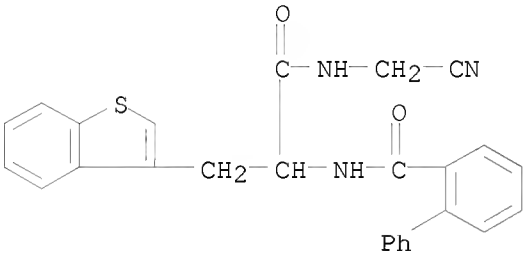
IT 713532-10-6P 713533-50-7P 713534-55-5P
713535-98-9P 713537-46-3P 713538-86-4P
713539-51-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid cyanoalkylamides as rotamase inhibitors)

RN 713532-10-6 CAPLUS

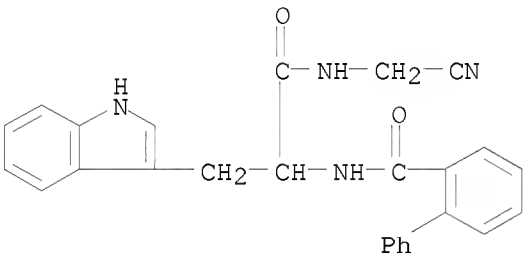
CN 2-Naphthalenepropanamide, α-[([1,1'-biphenyl]-2-ylcarbonyl)amino]-N-(cyanomethyl)- (CA INDEX NAME)



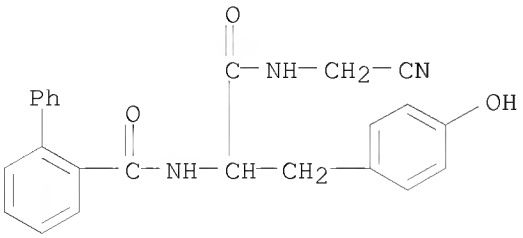
RN 713533-50-7 CAPLUS
CN Benzo[b]thiophene-3-propanamide, α-[([1,1'-biphenyl]-2-ylcarbonyl)amino]-N-(cyanomethyl)- (CA INDEX NAME)



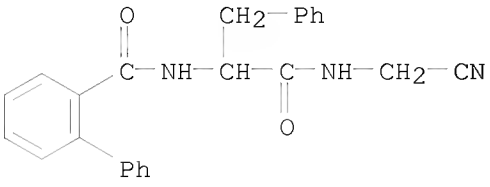
RN 713534-55-5 CAPLUS
CN 1H-Indole-3-propanamide, α-[([1,1'-biphenyl]-2-ylcarbonyl)amino]-N-(cyanomethyl)- (CA INDEX NAME)



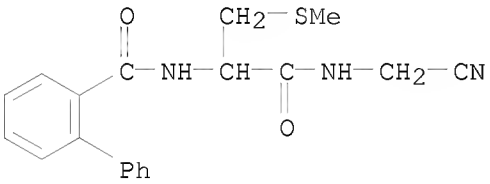
RN 713535-98-9 CAPLUS
CN Benzenepropanamide, α-[([1,1'-biphenyl]-2-ylcarbonyl)amino]-N-(cyanomethyl)-4-hydroxy- (CA INDEX NAME)



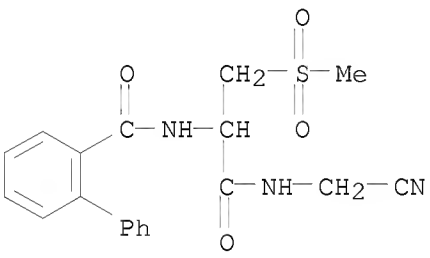
RN 713537-46-3 CAPLUS
CN Benzenepropanamide, α-[([1,1'-biphenyl]-2-ylcarbonyl)amino]-N-(cyanomethyl)- (CA INDEX NAME)



RN 713538-86-4 CAPLUS
CN [1,1'-Biphenyl]-2-carboxamide, N-[2-[(cyanomethyl)amino]-1-[(methylthio)methyl]-2-oxoethyl]- (CA INDEX NAME)



RN 713539-51-6 CAPLUS
CN [1,1'-Biphenyl]-2-carboxamide, N-[2-[(cyanomethyl)amino]-1-[(methylsulfonyl)methyl]-2-oxoethyl]- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 28 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:525096 CAPLUS
DOCUMENT NUMBER: 141:89363
TITLE: Preparation of amino acid cyanoalkylamides as rotamase inhibitors
INVENTOR(S): Knolle, Jochen; Schutkowski, Mike; Hummel, Gerd
PATENT ASSIGNEE(S): Jerini A.-G., Germany
SOURCE: Eur. Pat. Appl., 126 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1433778	A1	20040630	EP 2002-28699	20021223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
WO 2004065353	A1	20040805	WO 2003-EP14844	20031223
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003300552	A1	20040813	AU 2003-300552	20031223
EP 1575903	A1	20050921	EP 2003-815374	20031223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 20060252813	A1	20061109	US 2005-540013	20050622
PRIORITY APPLN. INFO.:			EP 2002-28699 A	20021223
			WO 2003-EP14844 W	20031223

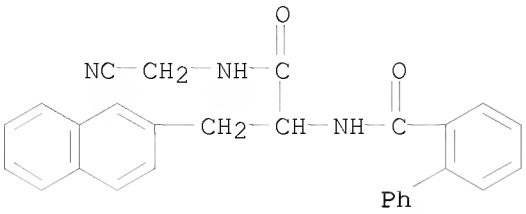
OTHER SOURCE(S): MARPAT 141:89363

AB The invention relates to compds. A-B-C-D [A is R1C(:Y)NR2 (Y is O, S, NH or substituted imino; R1, R2 are H, alkyl, aryl, etc.), R1O2CNR2, R1R2NC(:Y)NR2, R1SO2NR2, R1R2N, R1, or 1-azepinyl, 1-pyrrolidinyl or piperidino substituted by RxNHCO, where Rx is alkyl, an amino acid or peptide residue; B is absent or CR3R4C(:Y)NR5, where R3-R5 are groups defined by R1 or R2; C is CR6R7CR8R9 or CR6R7, where R6-R9 are groups defined by R1 or R2; D is a functional group such as formyl, cyano or acyl or functional group-substituted alkyl] or their pharmaceutically-acceptable salts or prodrugs for use as inhibitors of a rotamase. Examples illustrate syntheses of compds. of the invention via amidation reactions. EtNHC(S)NHCH(CH2C10H7-2)CONHCH2CH2CN (C10H7-2 = 2-naphthyl) showed IC50 < 5 μM for inhibition of rotamase hPin1.

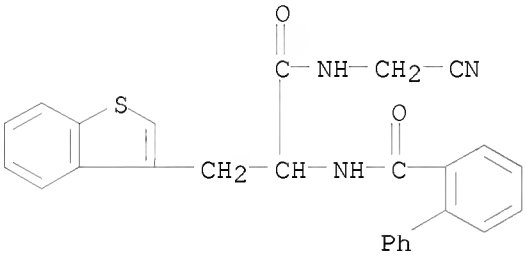
IT 713532-10-6P 713533-50-7P 713534-55-5P
713535-98-9P 713537-46-3P 713538-86-4P
713539-51-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid cyanoalkylamides as rotamase inhibitors)

RN 713532-10-6 CAPLUS

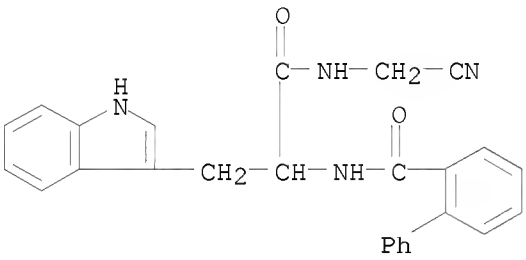
CN 2-Naphthalenepropanamide, α-[([1,1'-biphenyl]-2-ylcarbonyl)amino]-N-(cyanomethyl)- (CA INDEX NAME)



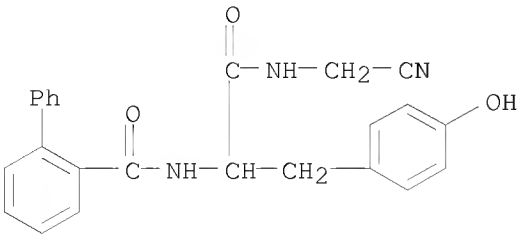
RN 713533-50-7 CAPLUS
CN Benzo[b]thiophene-3-propanamide, α-[([1,1'-biphenyl]-2-ylcarbonyl)amino]-N-(cyanomethyl)- (CA INDEX NAME)



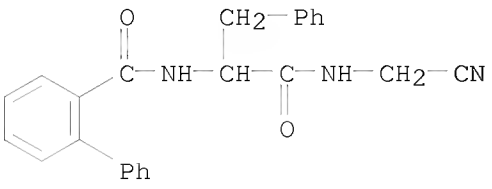
RN 713534-55-5 CAPLUS
CN 1H-Indole-3-propanamide, α-[([1,1'-biphenyl]-2-ylcarbonyl)amino]-N-(cyanomethyl)- (CA INDEX NAME)



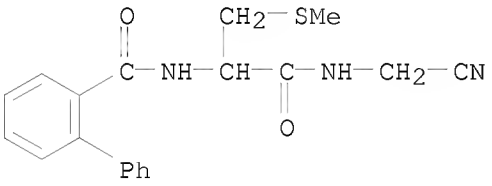
RN 713535-98-9 CAPLUS
CN Benzenepropanamide, α-[([1,1'-biphenyl]-2-ylcarbonyl)amino]-N-(cyanomethyl)-4-hydroxy- (CA INDEX NAME)



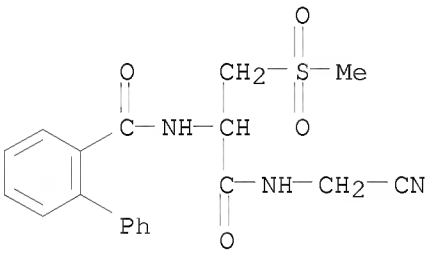
RN 713537-46-3 CAPLUS
CN Benzenepropanamide, α-[([1,1'-biphenyl]-2-ylcarbonyl)amino]-N-(cyanomethyl)- (CA INDEX NAME)



RN 713538-86-4 CAPLUS
CN [1,1'-Biphenyl]-2-carboxamide, N-[2-[(cyanomethyl)amino]-1-[(methylthio)methyl]-2-oxoethyl]- (CA INDEX NAME)



RN 713539-51-6 CAPLUS
CN [1,1'-Biphenyl]-2-carboxamide, N-[2-[(cyanomethyl)amino]-1-[(methylsulfonyl)methyl]-2-oxoethyl]- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

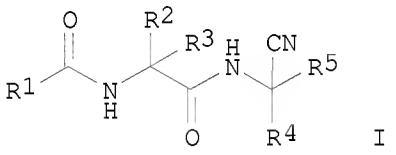
L4 ANSWER 29 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:515539 CAPLUS
DOCUMENT NUMBER: 141:71829
TITLE: Cyanomethyl derivatives as cysteine protease inhibitors
INVENTOR(S): Graupe, Michael; Lau, Agnes J.; Link, John O.; Liu, Yang; Mossman, Craig J.; Patterson, John W.; Zipfel, Sheila M.
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 134 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004052921	A1	20040624	WO 2003-US37979	20031126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2506114	A1	20040624	CA 2003-2506114	20031126
AU 2003298740	A1	20040630	AU 2003-298740	20031126
EP 1569954	A1	20050907	EP 2003-796499	20031126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 20060122184	A1	20060608	US 2005-536889	20051017

PRIORITY APPLN. INFO.: US 2002-431354P P 20021205
WO 2003-US37979 W 20031126

OTHER SOURCE(S): MARPAT 141:71829
GI



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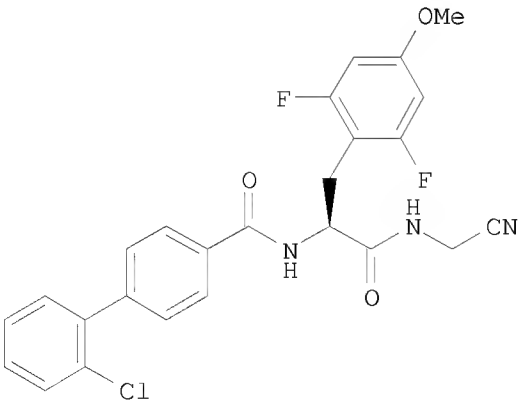


II

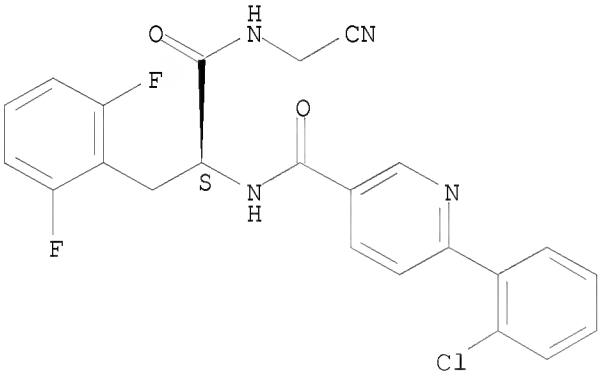
AB The dipeptide derivs. [I [R1 = substituted Ph, aryl, diaryl, heterodiaryl, furanyl, arylfuranyl, pyrazolyl, etc.; R2 = H, (un)substituted cycloalkyl, indolyl, alkylindolyl, Me, Et, Pr, pentyl, etc.; R3 = H, or R2 and R3 together with the carbon atom to which they are attached formed (un)substituted cycloalkylene, cycloalkenylene or spirocycloalkylene; R4 = H; R5 = H, (un)substituted alkyl or heteroaryl, or R4 and R5 together with the carbon atom to which they are attached form cycloalkylene or heterocycloalkylene]] were prepared as cysteine protease inhibitors, in particular, cathepsins B, K, L, F, and S, for treating diseases mediated by these proteases. Thus, compound II was prepared via peptide coupling of 2'-chlorobiphenyl-4-carboxylic acid with synthesized 2(S)-amino-N-cyanomethyl-3-(2,6-difluoro-4-methoxyphenyl)-propionamide. Compds. of the invention were tested by in vitro essays for protease activity and showed cathepsins B, K, L, F, and S inhibitory activity.

IT 710350-01-9P 710350-03-1P 710350-04-2P
710350-05-3P 710350-06-4P 710350-07-5P
710350-08-6P 710350-11-1P 710350-12-2P
710350-14-4P 710350-15-5P 710350-20-2P
710350-21-3P 710350-22-4P 710350-23-5P
710350-24-6P 710350-25-7P 710350-31-5P
710350-32-6P 710350-33-7P 710350-34-8P
710350-35-9P 710350-36-0P 710350-37-1P
710350-38-2P 710350-39-3P 710350-80-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of dipeptide cyanomethyl derivs. as cysteine protease inhibitors)

RN 710350-01-9 CAPLUS

CN 3-Pyridinecarboxamide, 6-(2-chlorophenyl)-N-[(1S)-2-[(cyanomethyl)amino]-1-[(2,6-difluorophenyl)methyl]-2-oxoethyl]- (CA INDEX NAME)

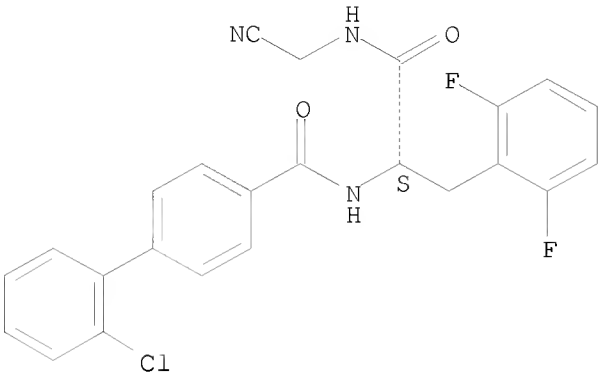
Absolute stereochemistry.



RN 710350-03-1 CAPLUS

CN Benzenepropanamide, α-[[(2'-chloro[1,1'-biphenyl]-4-yl)carbonyl]amino]-N-(cyanomethyl)-2,6-difluoro-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.



RN 710350-04-2 CAPLUS
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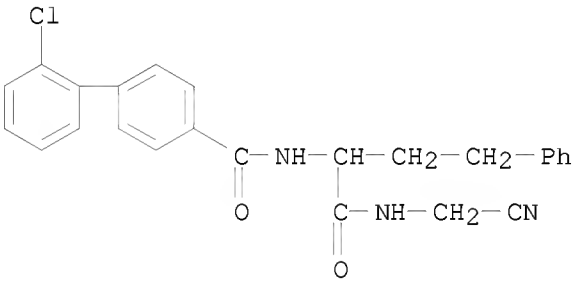
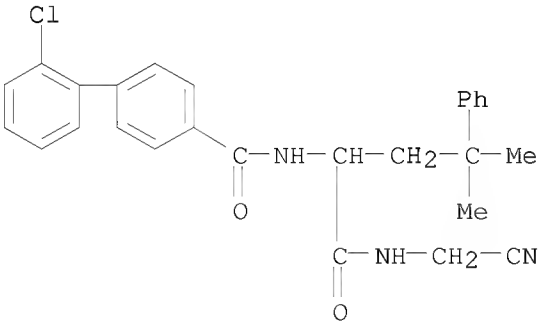
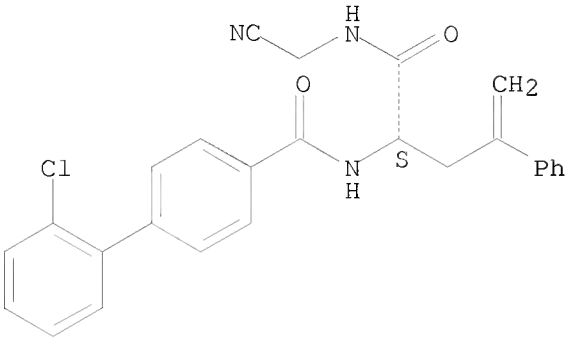


RN 710350-05-3 CAPLUS
CN Benzenebutanamide, α-[[(2'-chloro[1,1'-biphenyl]-4-yl)carbonyl]amino]-N-(cyanomethyl)-γ,γ-dimethyl- (CA INDEX NAME)



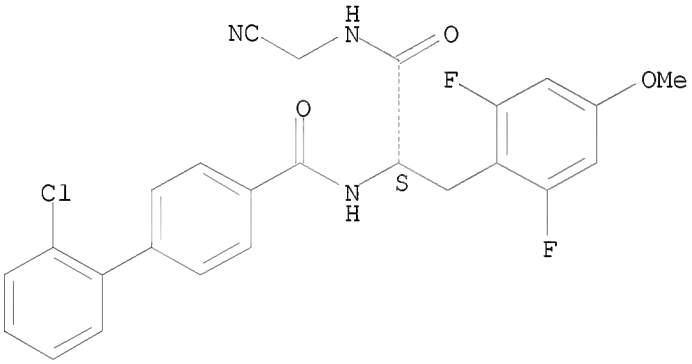
RN 710350-06-4 CAPLUS
CN Benzenebutanamide, α-[[(2'-chloro[1,1'-biphenyl]-4-yl)carbonyl]amino]-N-(cyanomethyl)-γ-methylene-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.



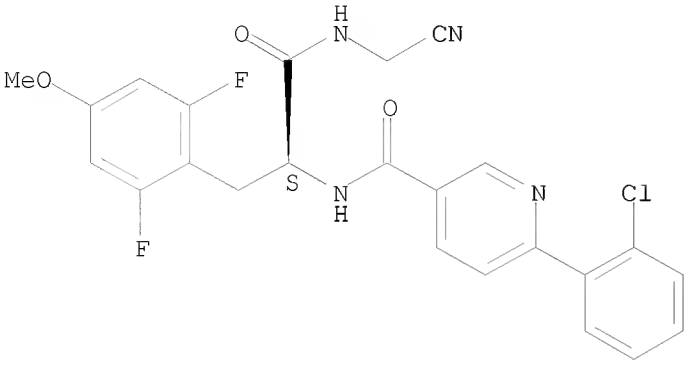
RN 710350-07-5 CAPLUS
CN Benzenepropanamide, α-[[(2'-chloro[1,1'-biphenyl]-4-yl)carbonyl]amino]-N-(cyanomethyl)-2,6-difluoro-4-methoxy-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.



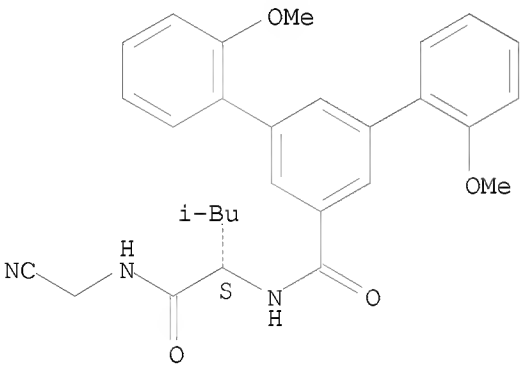
RN 710350-08-6 CAPLUS
CN 3-Pyridinecarboxamide, 6-(2-chlorophenyl)-N-[(1S)-2-[(cyanomethyl)amino]-1-[(2,6-difluoro-4-methoxyphenyl)methyl]-2-oxoethyl]- (CA INDEX NAME)

Absolute stereochemistry.



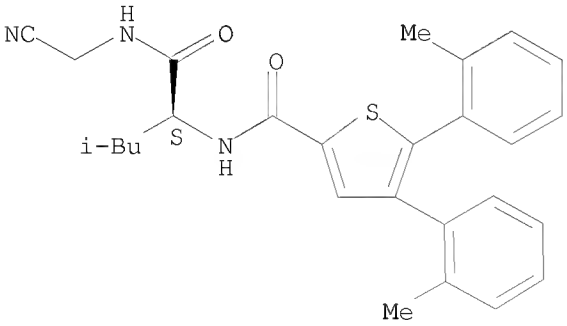
RN 710350-11-1 CAPLUS
CN [1,1':3',1''-Terphenyl]-5'-carboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-2,2''-dimethoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



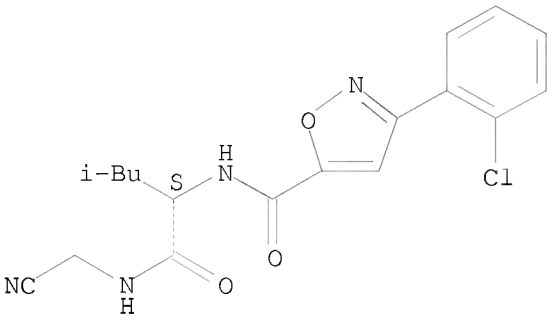
RN 710350-12-2 CAPLUS
CN 2-Thiophenecarboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4,5-bis(2-methylphenyl)- (CA INDEX NAME)

Absolute stereochemistry.



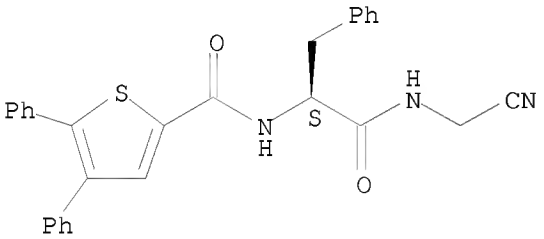
RN 710350-14-4 CAPLUS
CN 5-Isoxazolecarboxamide, 3-(2-chlorophenyl)-N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]- (CA INDEX NAME)

Absolute stereochemistry.



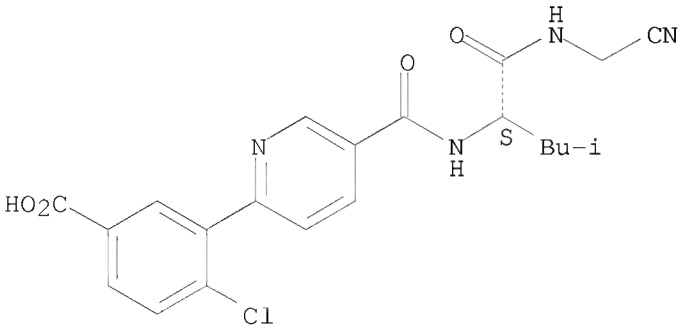
RN 710350-15-5 CAPLUS
CN 2-Thiophenecarboxamide, N-[(1S)-2-[(cyanomethyl)amino]-2-oxo-1-(phenylmethyl)ethyl]-4,5-diphenyl- (CA INDEX NAME)

Absolute stereochemistry.



RN 710350-20-2 CAPLUS
CN Benzoic acid, 4-chloro-3-[5-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]-2-pyridinyl]- (CA INDEX NAME)

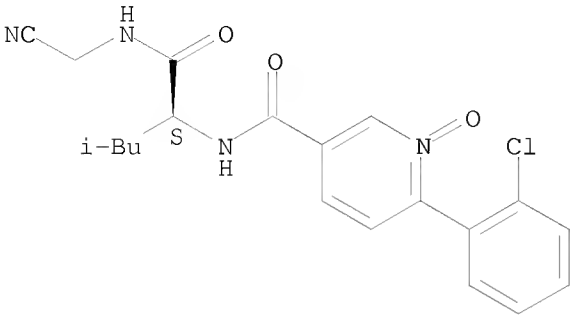
Absolute stereochemistry.



RN 710350-21-3 CAPLUS
CN 3-Pyridinecarboxamide, 6-(2-chlorophenyl)-N-[(1S)-1-

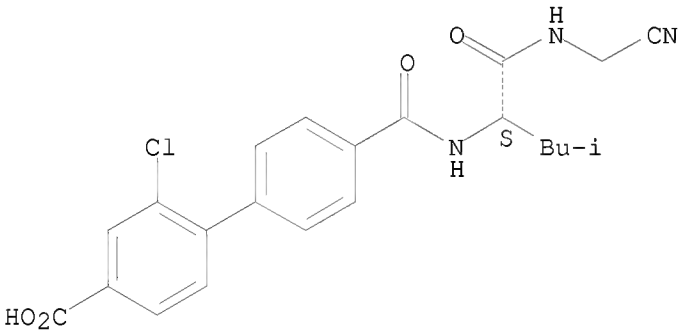
[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-, 1-oxide (CA INDEX NAME)

Absolute stereochemistry.



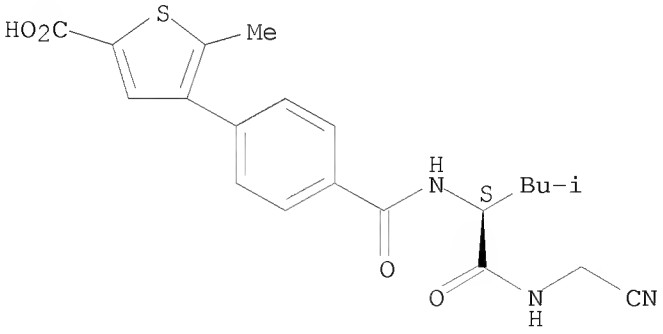
RN 710350-22-4 CAPLUS
CN [1,1'-Biphenyl]-4-carboxylic acid, 2-chloro-4'-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



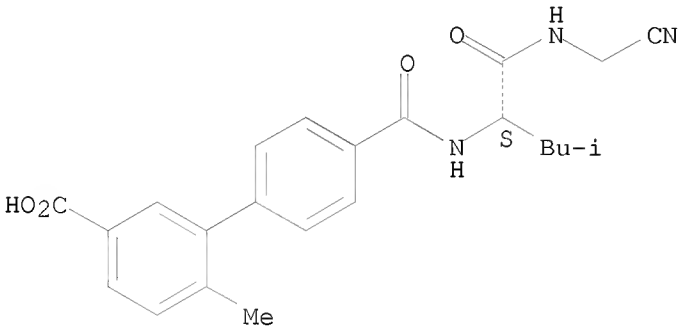
RN 710350-23-5 CAPLUS
CN 2-Thiophenecarboxylic acid, 4-[4-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-5-methyl- (CA INDEX NAME)

Absolute stereochemistry.



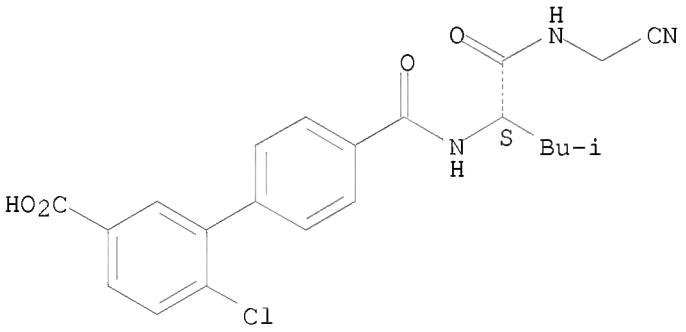
RN 710350-24-6 CAPLUS
CN [1,1'-Biphenyl]-3-carboxylic acid,
4'-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]-
6-methyl- (CA INDEX NAME)

Absolute stereochemistry.



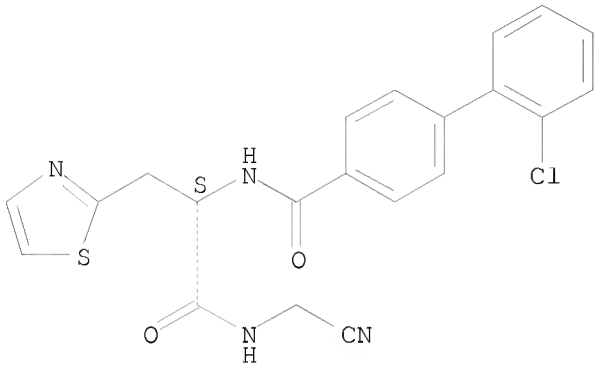
RN 710350-25-7 CAPLUS
CN [1,1'-Biphenyl]-3-carboxylic acid,
6-chloro-4'-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-
methylbutyl]amino]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



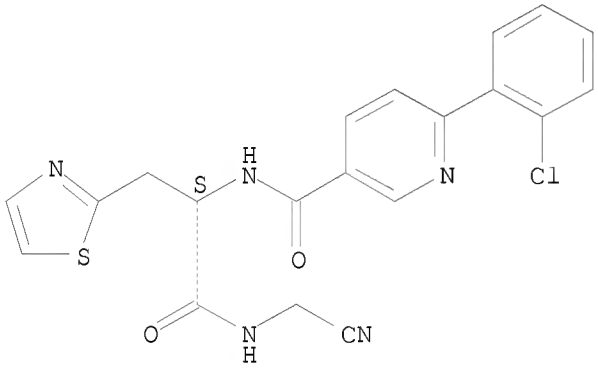
RN 710350-31-5 CAPLUS
CN 2-Thiazolepropanamide, α-[[(2'-chloro[1,1'-biphenyl]-4-
yl)carbonyl]amino]-N-(cyanomethyl)-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.



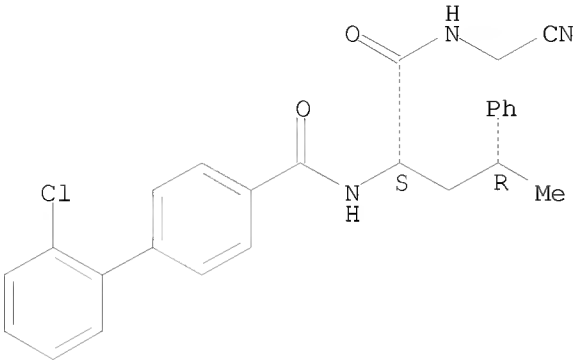
RN 710350-32-6 CAPLUS
CN 3-Pyridinecarboxamide, 6-(2-chlorophenyl)-N-[(1S)-2-[(cyanomethyl)amino]-2-oxo-1-(2-thiazolylmethyl)ethyl]- (CA INDEX NAME)

Absolute stereochemistry.



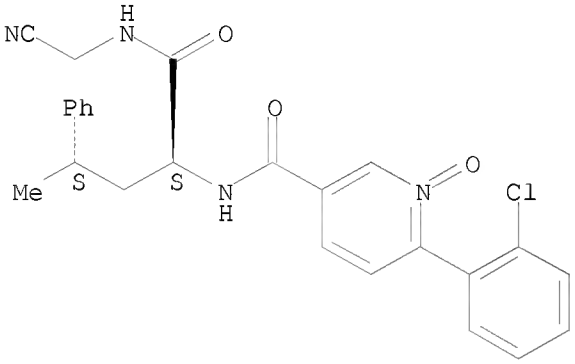
RN 710350-33-7 CAPLUS
CN Benzenebutanamide, α-[[(2'-chloro[1,1'-biphenyl]-4-yl)carbonyl]amino]-N-(cyanomethyl)-γ-methyl-, (αS,γR)- (CA INDEX NAME)

Absolute stereochemistry.



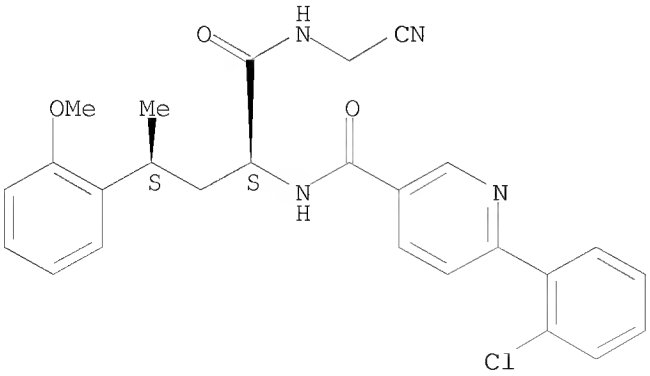
RN 710350-34-8 CAPLUS
CN 3-Pyridinecarboxamide, 6-(2-chlorophenyl)-N-[(1S,3S)-1-[[(cyanomethyl)amino]carbonyl]-3-phenylbutyl]-, 1-oxide (CA INDEX NAME)

Absolute stereochemistry.



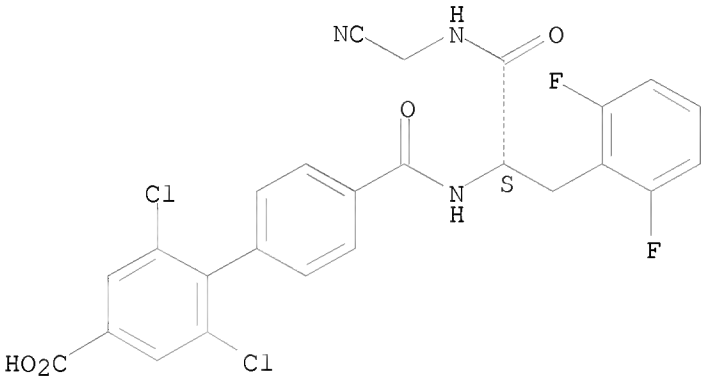
RN 710350-35-9 CAPLUS
CN 3-Pyridinecarboxamide, 6-(2-chlorophenyl)-N-[(1S,3S)-1-[[(cyanomethyl)amino]carbonyl]-3-(2-methoxyphenyl)butyl]- (CA INDEX NAME)

Absolute stereochemistry.



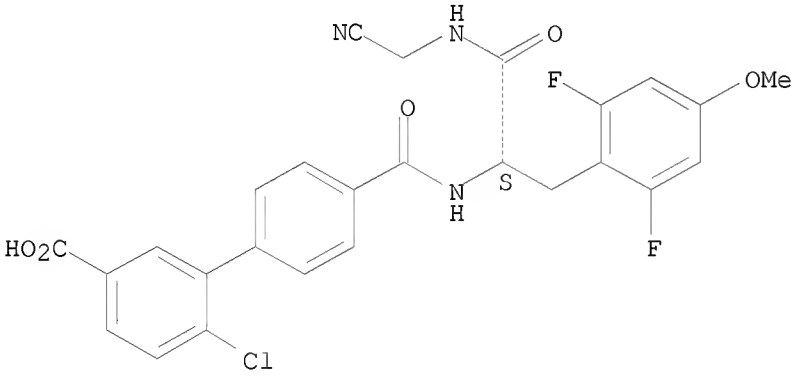
RN 710350-36-0 CAPLUS
CN [1,1'-Biphenyl]-4-carboxylic acid, 2,6-dichloro-4'-[[[(1S)-2-[(cyanomethyl)amino]-1-[(2,6-difluorophenyl)methyl]-2-oxoethyl]amino]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



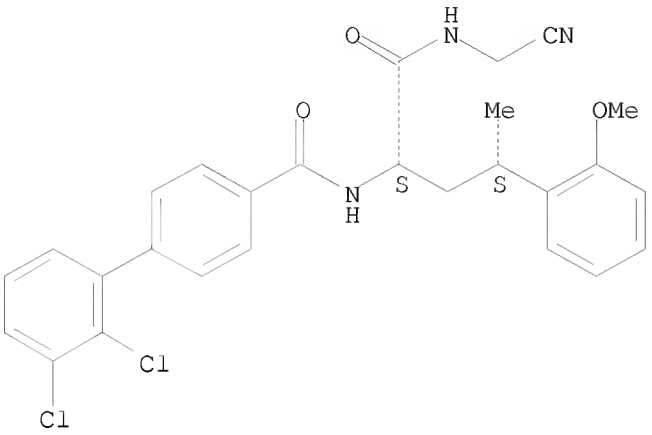
RN 710350-37-1 CAPLUS
CN [1,1'-Biphenyl]-3-carboxylic acid, 6-chloro-4'-[[[(1S)-2-[(cyanomethyl)amino]-1-[(2,6-difluoro-4-methoxyphenyl)methyl]-2-oxoethyl]amino]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



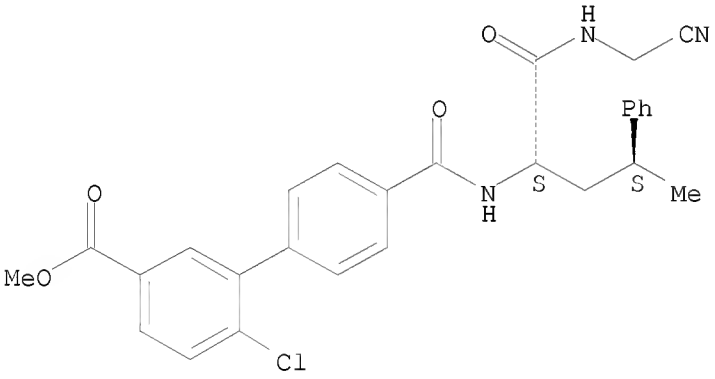
RN 710350-38-2 CAPLUS
CN Benzenebutanamide, N-(cyanomethyl)-α-[[(2',3'-dichloro[1,1'-biphenyl]-4-yl)carbonyl]amino]-2-methoxy-γ-methyl-, (αS,γS)- (CA INDEX NAME)

Absolute stereochemistry.



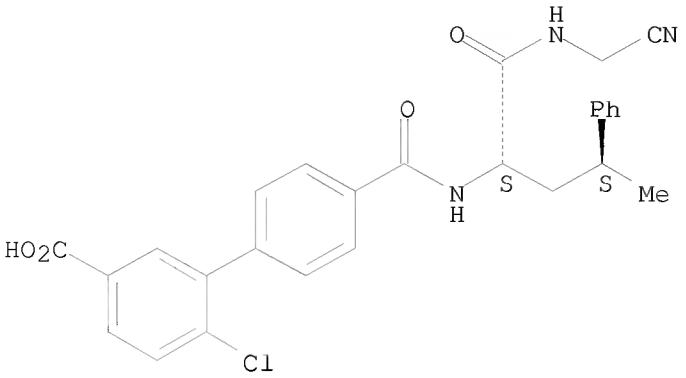
RN 710350-39-3 CAPLUS
CN [1,1'-Biphenyl]-3-carboxylic acid, 6-chloro-4'-[[[(1S,3S)-1-[[(cyanomethyl)amino]carbonyl]-3-phenylbutyl]amino]carbonyl]-, methyl ester (CA INDEX NAME)

Absolute stereochemistry.



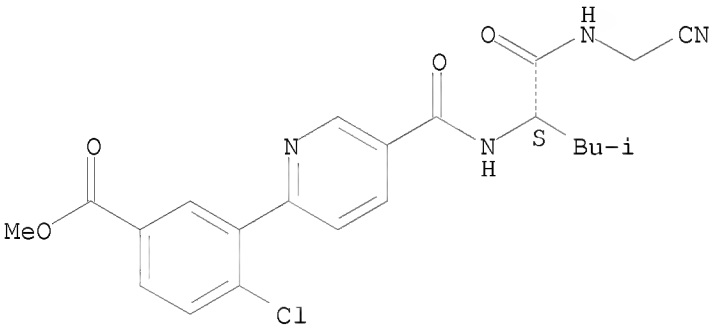
RN 710350-80-4 CAPLUS
CN [1,1'-Biphenyl]-3-carboxylic acid, 6-chloro-4'-[[[(1S,3S)-1-[[(cyanomethyl)amino]carbonyl]-3-phenylbutyl]amino]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.



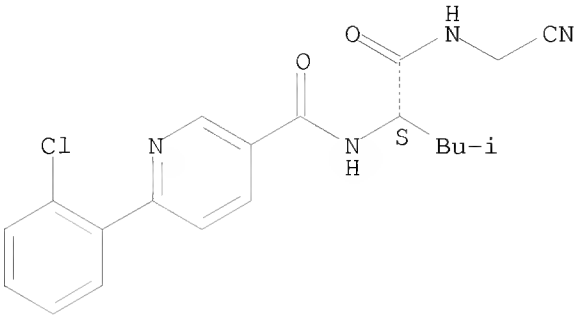
IT 710350-73-5P 710350-74-6P 710350-76-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of dipeptide cyanomethyl derivs. as cysteine protease inhibitors)
RN 710350-73-5 CAPLUS
CN Benzoic acid, 4-chloro-3-[5-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]-2-pyridinyl]-, methyl ester (CA INDEX NAME)

Absolute stereochemistry.



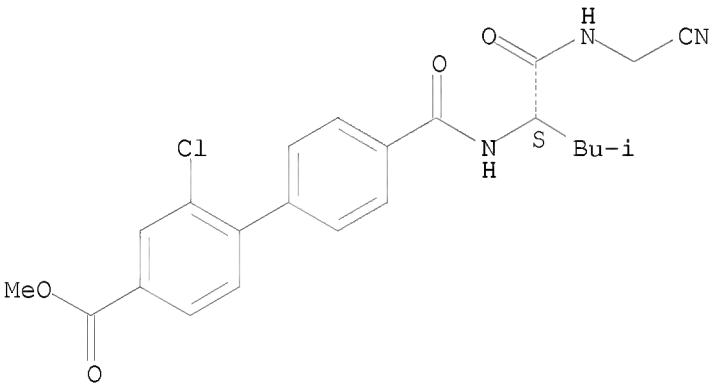
RN 710350-74-6 CAPLUS
CN 3-Pyridinecarboxamide, 6-(2-chlorophenyl)-N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 710350-76-8 CAPLUS
CN [1,1'-Biphenyl]-4-carboxylic acid, 2-chloro-4'-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]-, methyl ester (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 30 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:267319 CAPLUS
DOCUMENT NUMBER: 140:304079
TITLE: Preparation of iodotyrosine cyanomethylamides as Cathepsin B inhibitors
INVENTOR(S): Burrill, Leland C., II; Palmer, James T.; Rydzewski, Robert M.
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026851	A1	20040401	WO 2003-US29545	20030916
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2498149	A1	20040401	CA 2003-2498149		20030916
AU 2003282804	A1	20040408	AU 2003-282804		20030916
EP 1539725	A1	20050615	EP 2003-774482		20030916
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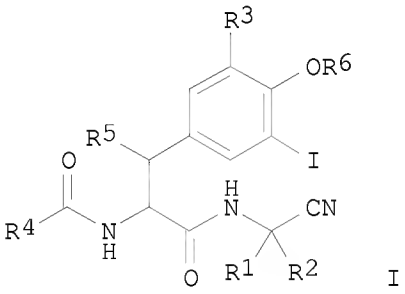
US 20050282871	A1	20051222	US 2005-528266		20050317
PRIORITY APPLN. INFO.:			US 2002-412368P	P	20020920
			WO 2003-US29545	W	20030916

OTHER SOURCE(S): MARPAT 140:304079
GI



I

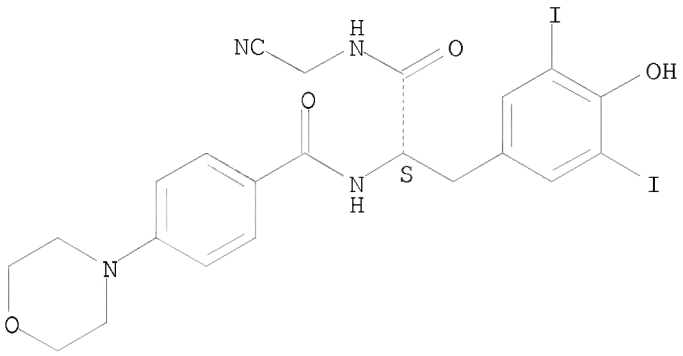
AB Title compds. [I; R1, R2 = H, alkyl, haloalkyl, hydroxyalkyl, aryl, aralkyl; R1R2 = atoms to form a cycloalkyl, heterocycloalkyl ring; R3 = alkyl, iodo; R4 = (substituted) aryl, heteroaryl, heterocycloalkyl; R5, R6 = H, alkyl], were prepared as Cathepsin B inhibitors (no data). Thus, 4-morpholinobenzoic acid hydrochloride, hydroxybenzotriazole, Et3N, and EDC were stirred 30 min in DMF; L-3,5-diiodotyrosine, Et3N, and H2O in DMF were added followed by stirring for 16 h to give (S)-3-(4-hydroxy-3,5-diiodophenyl)-2-(4-morpholin-4-ylbenzoylamino)propionic acid. The latter was stirred overnight with aminoacetonitrile hydrochloride, HBTU, and N-methylmorpholine in DMF to give (S)-N-[1-(cyanomethylcarbamoyl)-2-(4-hydroxy-3,5-diiodophenyl)ethyl]-4-morpholin-4-ylbenzamide.

IT 676477-45-5P, (S)-N-[1-(Cyanomethylcarbamoyl)-2-(4-hydroxy-3,5-diiodophenyl)ethyl]-4-morpholin-4-ylbenzamide 676477-48-8P 676477-53-5P 676477-54-6P 676477-55-7P 676477-63-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of iodotyrosine cyanomethylamides as Cathepsin B inhibitors)

RN 676477-45-5 CAPLUS

CN Benzenepropanamide, N-(cyanomethyl)-4-hydroxy-3,5-diiodo-α-[[4-(4-morpholinyl)benzoyl]amino]-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.

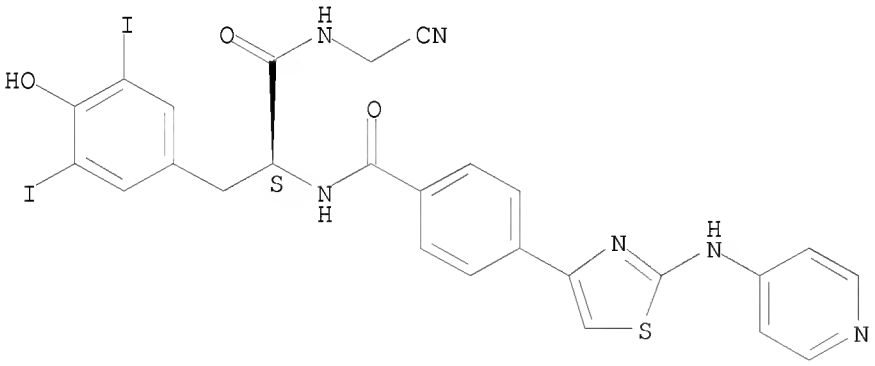


RN 676477-48-8 CAPLUS
CN Benzenepropanamide, N-(cyanomethyl)-4-hydroxy-3,5-diiodo-α-[[4-[2-(4-pyridinylamino)-4-thiazolyl]benzoyl]amino]-, (αS)-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

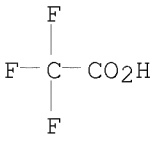
CRN 676477-47-7
CMF C26 H20 I2 N6 O3 S

Absolute stereochemistry.



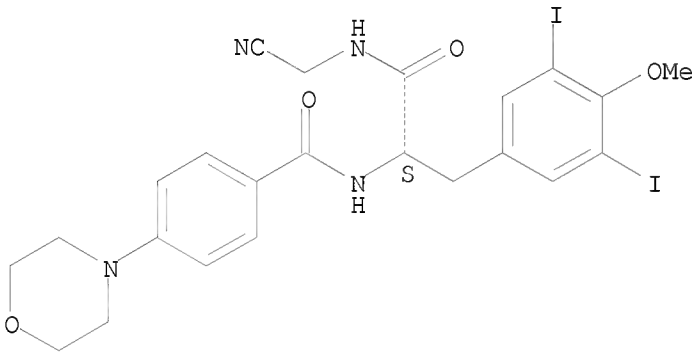
CM 2

CRN 76-05-1
CMF C2 H F3 O2



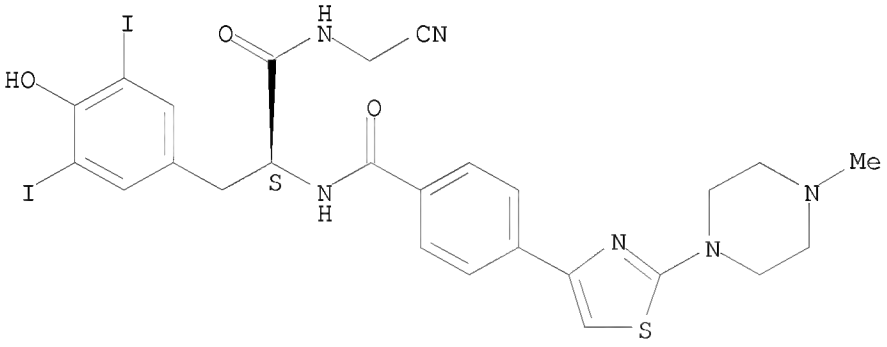
RN 676477-53-5 CAPLUS
CN Benzenepropanamide, N-(cyanomethyl)-3,5-diiodo-4-methoxy-α-[[4-(4-morpholinyl)benzoyl]amino]-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.



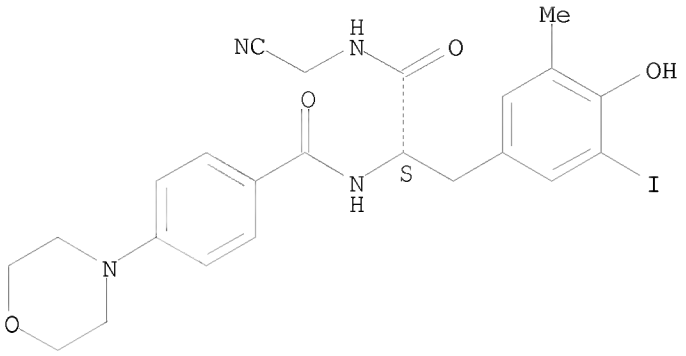
RN 676477-54-6 CAPLUS
CN Benzenepropanamide, N-(cyanomethyl)-4-hydroxy-3,5-diiodo-α-[[4-[2-(4-methyl-1-piperazinyl)-4-thiazolyl]benzoyl]amino]-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.



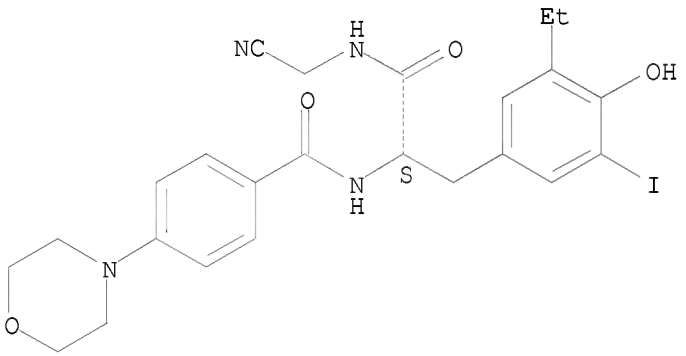
RN 676477-55-7 CAPLUS
CN Benzenepropanamide, N-(cyanomethyl)-4-hydroxy-3-iodo-5-methyl-α-[[4-(4-morpholinyl)benzoyl]amino]-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.



RN 676477-63-7 CAPLUS
CN Benzenepropanamide, N-(cyanomethyl)-3-ethyl-4-hydroxy-5-iodo-α-[[4-(4-morpholinyl)benzoyl]amino]-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 31 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:737516 CAPLUS
DOCUMENT NUMBER: 139:257284
TITLE: Cathepsin cysteine protease inhibitors and their therapeutic use
INVENTOR(S): Bayly, Christopher I.; Black, Cameron; Leger, Serge; Li, Chun Sing; McKay, Dan; Mellon, Christophe; Gauthier, Jacques Yves; Lau, Cheuk; Therien, Michel; Truong, Vouy-Linh; Green, Michael J.; Hirschbein, Bernard L.; Janc, James W.; Palmer, James T.; Baskaran, Chitra
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.; Axys Pharmaceuticals, Inc.
SOURCE: PCT Int. Appl., 282 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003075836	A2	20030918	WO 2003-US6147		20030228
WO 2003075836	A3	20040715			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
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AU 2003219953	A1	20030922	AU 2003-219953		20030228
AU 2003219953	B2	20071101			
US 20030232863	A1	20031218	US 2003-377377		20030228
EP 1482924	A2	20041208	EP 2003-716238		20030228
EP 1482924	B1	20080521			
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CN 1638757	A	20050713	CN 2003-805181		20030228
JP 2005526753	T	20050908	JP 2003-574112		20030228
NZ 534583	A	20061130	NZ 2003-534583		20030228
RU 2312861	C2	20071220	RU 2004-129587		20030228
AT 395911	T	20080615	AT 2003-716238		20030228
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US 20050240023	A1	20051027	US 2004-505796		20040825
US 7375134	B2	20080520			
IN 2004CN01940	A	20070720	IN 2004-CN1940		20040831
MX 2004PA08621	A	20041206	MX 2004-PA8621		20040903
NO 2004004207	A	20041124	NO 2004-4207		20041004
JP 2008115177	A	20080522	JP 2007-283678		20071031
US 20080188529	A1	20080807	US 2008-82104		20080408
PRIORITY APPLN. INFO.:			US 2002-361818P	P	20020305
			US 2002-408704P	P	20020906
			JP 2003-574112	A3	20030228
			WO 2003-US6147	W	20030228
			US 2004-505796	A3	20040825

OTHER SOURCE(S): MARPAT 139:257284

AB This invention relates to cysteine protease inhibitors R7(D)nCR6R7NR8CR3R4C(:O)NHCR1R2CN (R1-4 = H, (substituted)C1-6-alkyl or C2-6-alkenyl; R1 and R2 or R3 and R4 may be take together with the C atom to which they are attached to form a (substituted)C3-8-cycloalkyl or heterocyclic ring; R5 = H, (substituted)C1-6-alkyl; R6 = (substituted)aryl, heteroaryl, C1-6-haloalkyl, arylalky, heteroarylalkyl; D = (substituted)C1-3-alkyl, C2-3-alkenyl, C2-3-alkynyl, aryl, heteroaryl, C3-8-cycloalkyl, heterocyclyl; R7 = H, (substituted)C1-6-alkyl, C2-6-alkenyl, C2-6-alkynyl, C1-6-alkyloxy, etc.; R8 = H, C2-6-alkyl) including but not limited to, inhibitors of cathepsins K, L, S and B. These compds. are useful for treating diseases in which inhibition of bone

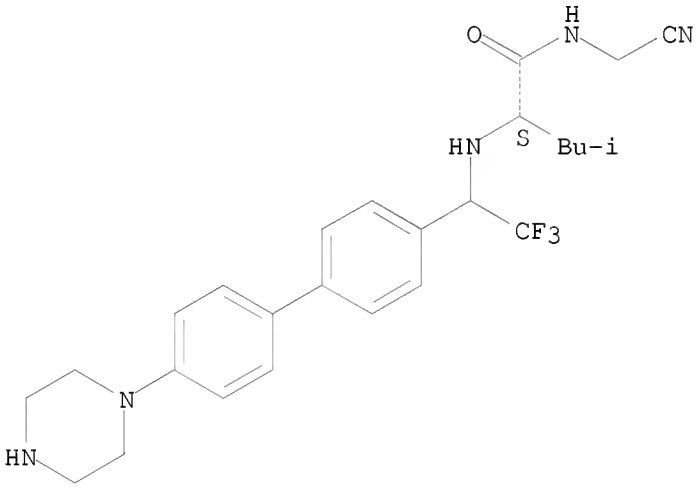
resorption is indicated, such as osteoporosis.

IT 603139-07-7P 603139-08-8P 603139-09-9P
603139-10-2P 603139-11-3P 603139-12-4P
603139-13-5P 603139-15-7P 603139-22-6P
603139-23-7P 603139-24-8P 603139-28-2P
603139-29-3P 603139-30-6P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cathepsin cysteine protease inhibitors and their therapeutic use)

RN 603139-07-7 CAPLUS

CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4'-(1-piperazinyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

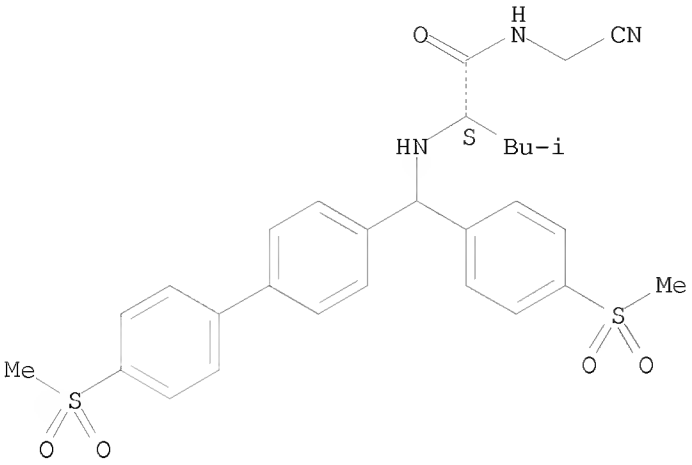
Absolute stereochemistry.



RN 603139-08-8 CAPLUS

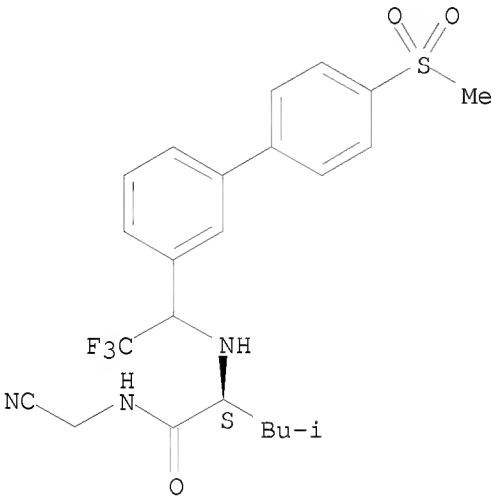
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl][4-(methylsulfonyl)phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



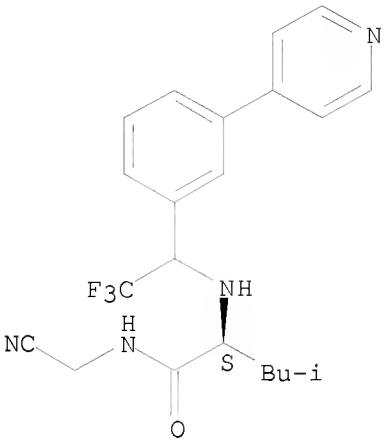
RN 603139-09-9 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-3-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



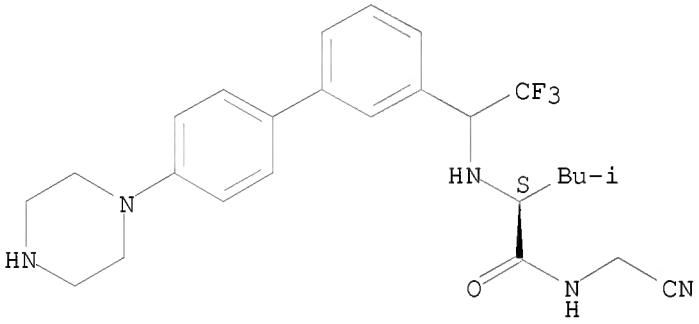
RN 603139-10-2 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[3-(4-pyridinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



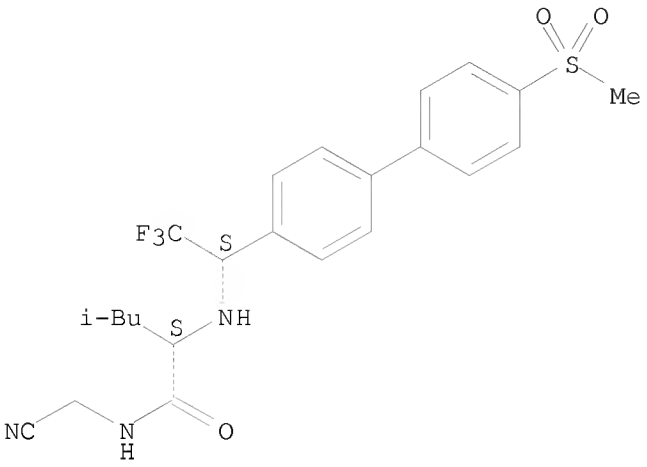
RN 603139-11-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4'-(1-piperazinyl)[1,1'-biphenyl]-3-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



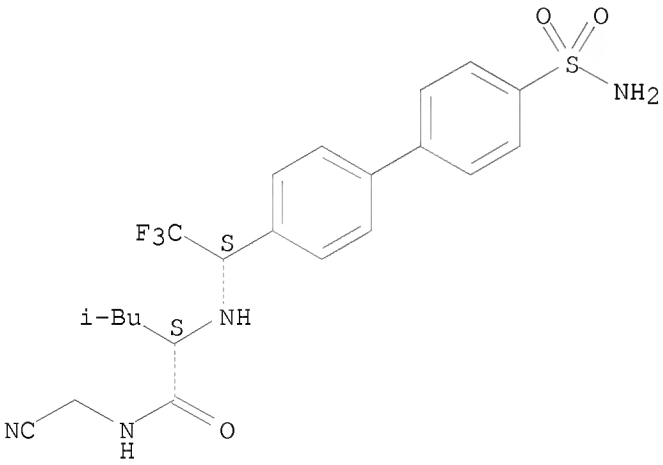
RN 603139-12-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



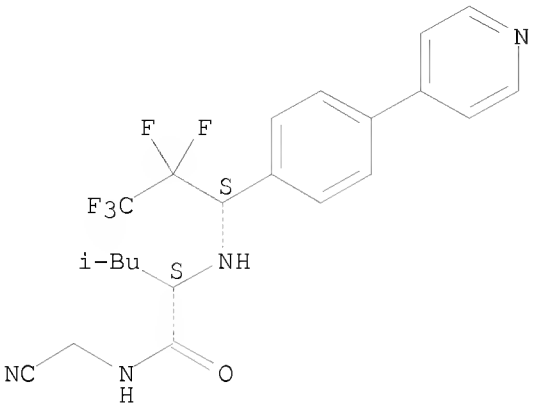
RN 603139-13-5 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4'-(aminosulfonyl)[1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



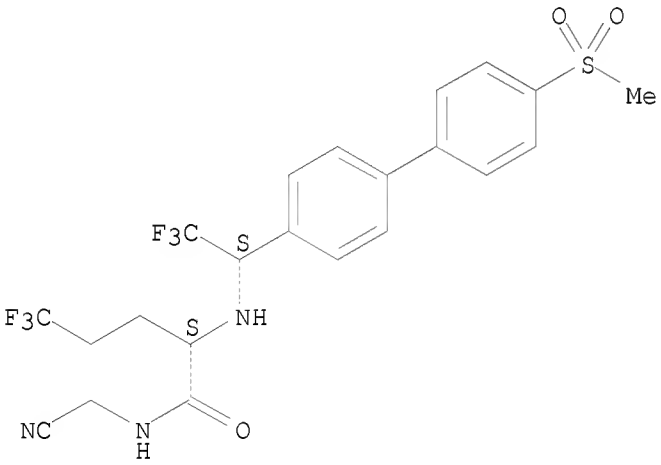
RN 603139-15-7 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,3,3,3-pentafluoro-1-[4-(4-pyridinyl)phenyl]propyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



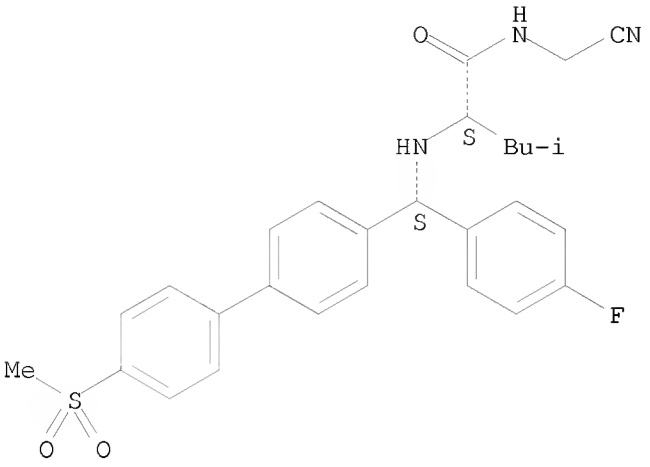
RN 603139-22-6 CAPLUS
CN Pentanamide, N-(cyanomethyl)-5,5,5-trifluoro-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



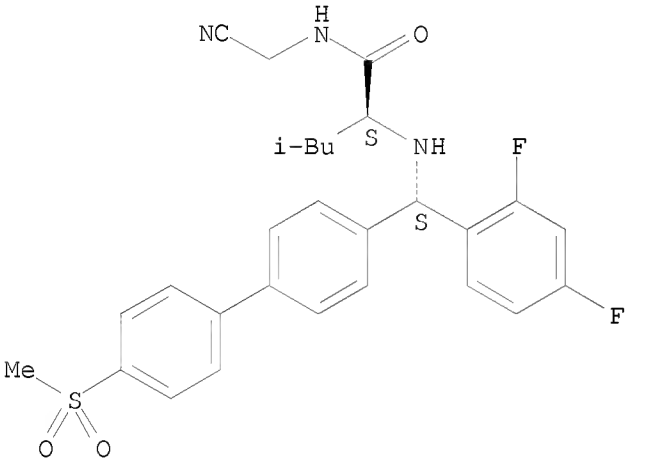
RN 603139-23-7 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[(S)-(4-fluorophenyl)[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]methyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



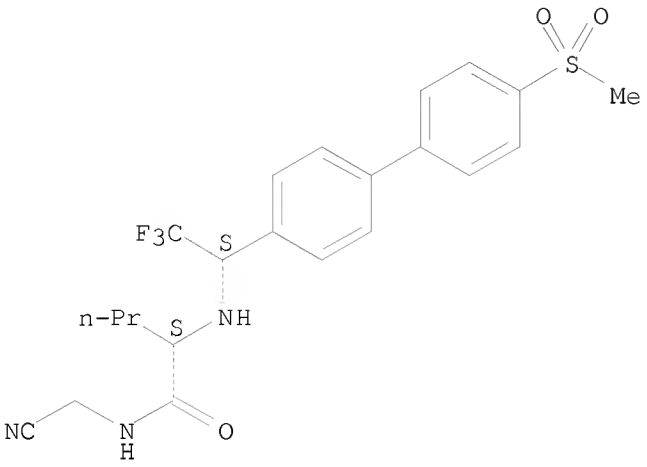
RN 603139-24-8 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[(S)-(2,4-difluorophenyl)[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]methyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



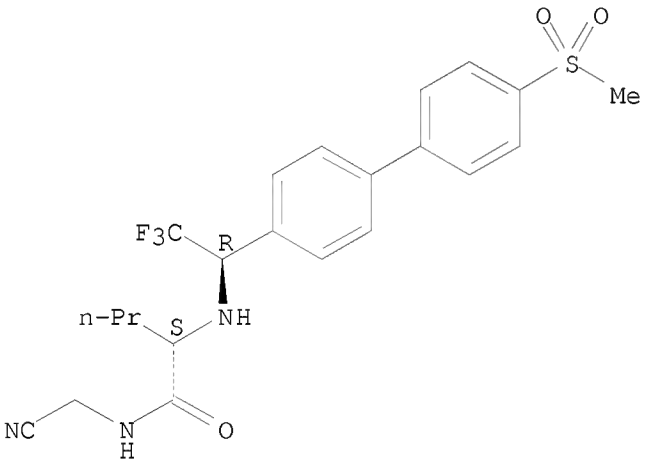
RN 603139-28-2 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



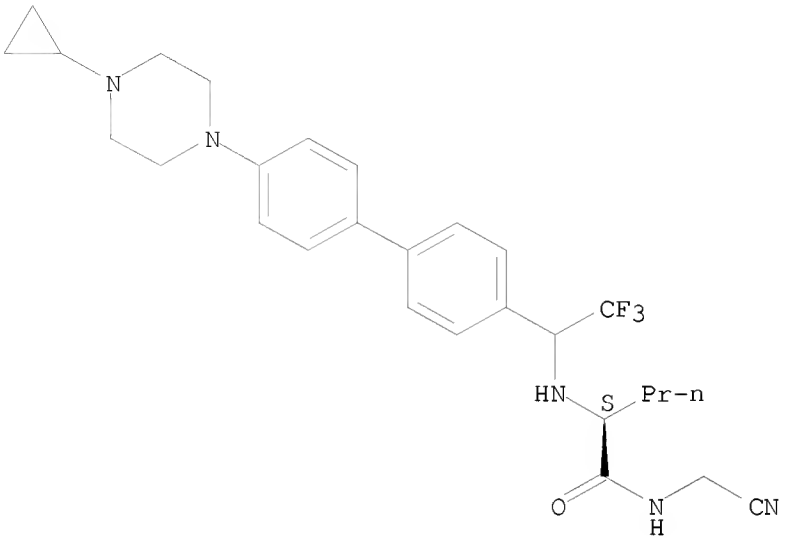
RN 603139-29-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[(1R)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



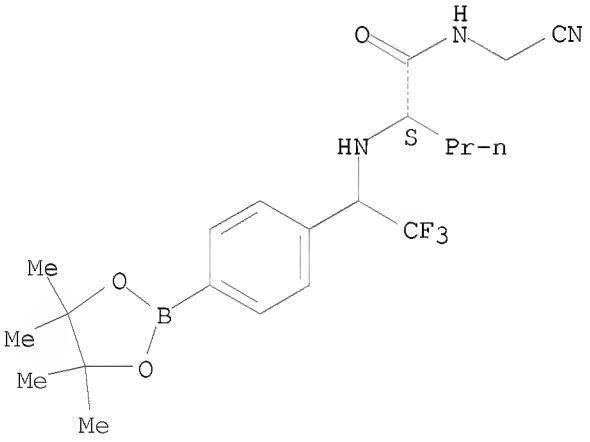
RN 603139-30-6 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[1-[4'-(4-cyclopropyl-1-piperazinyl)[1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



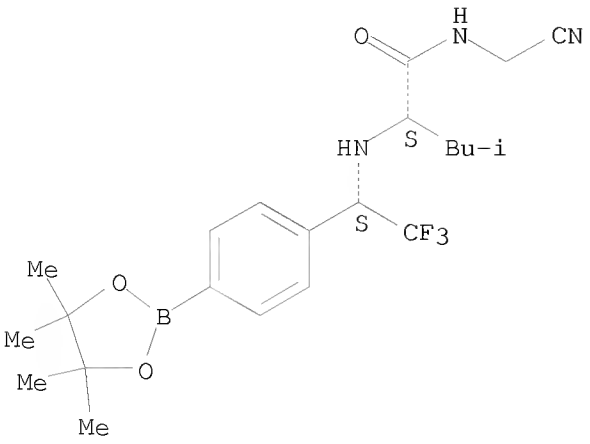
IT 603143-32-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(cathepsin cysteine protease inhibitors and their therapeutic use)
RN 603143-32-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[2,2,2-trifluoro-1-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 603142-84-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(cathepsin cysteine protease inhibitors and their therapeutic use)
RN 603142-84-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



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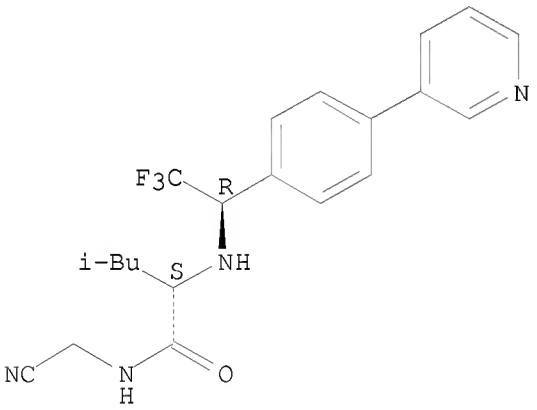
603142-70-7P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cathepsin cysteine protease inhibitors and their therapeutic use)

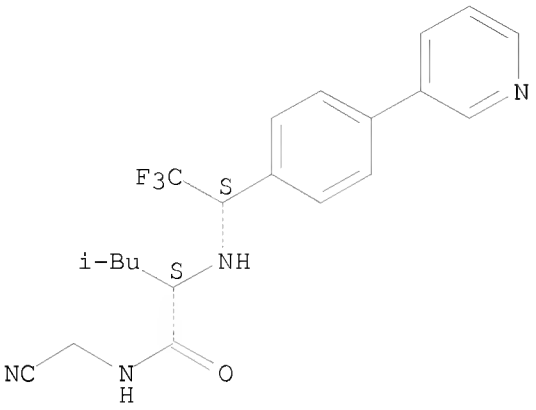
RN 603139-44-2 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1R)-2,2,2-trifluoro-1-[4-(3-pyridinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



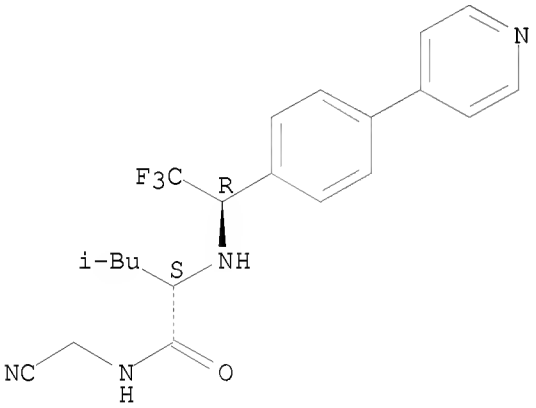
RN 603139-45-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(3-pyridinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



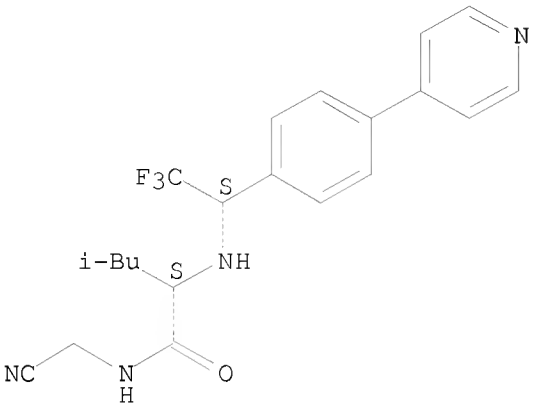
RN 603139-46-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1R)-2,2,2-trifluoro-1-[4-(4-pyridinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



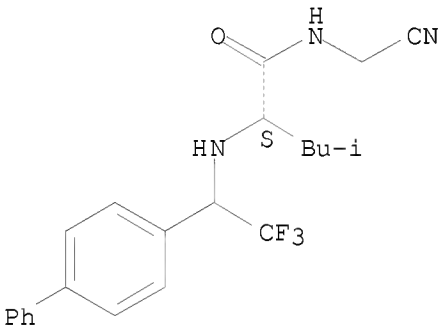
RN 603139-47-5 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(4-pyridinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



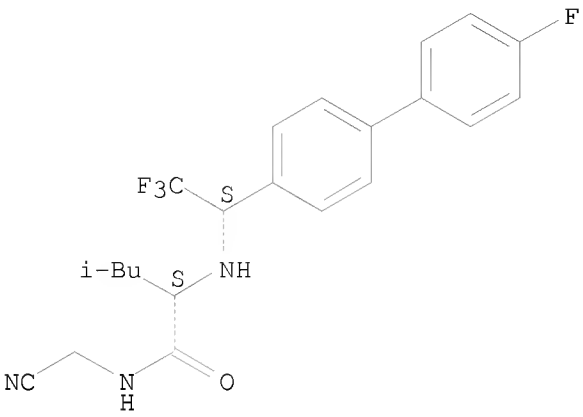
RN 603139-50-0 CAPLUS
CN Pentanamide, 2-[(1-[1,1'-biphenyl]-4-yl-2,2,2-trifluoroethyl)amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



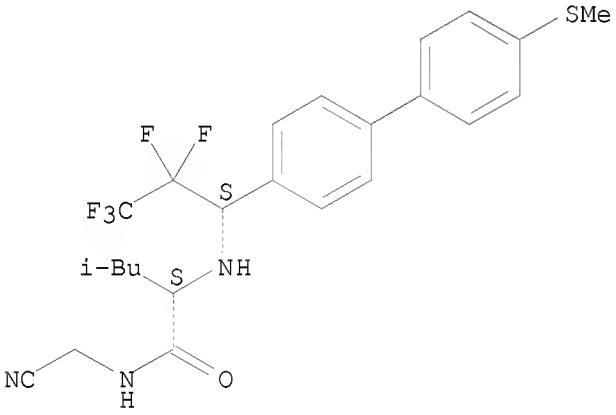
RN 603139-54-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-(4'-fluoro[1,1'-biphenyl]-4-yl)ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



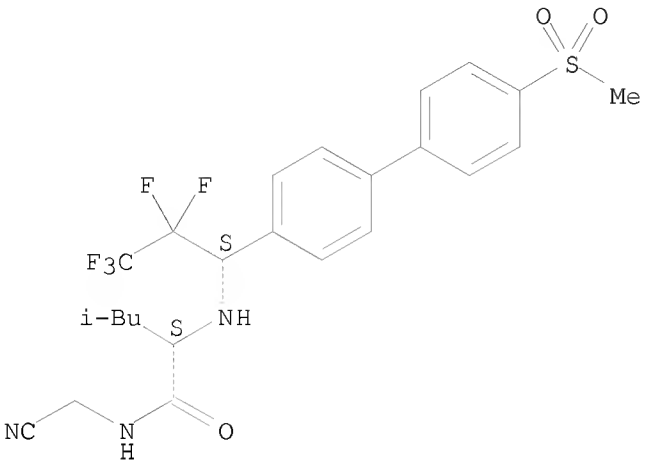
RN 603139-56-6 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,3,3,3-pentafluoro-1-[4'-(methylthio)[1,1'-biphenyl]-4-yl]propyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



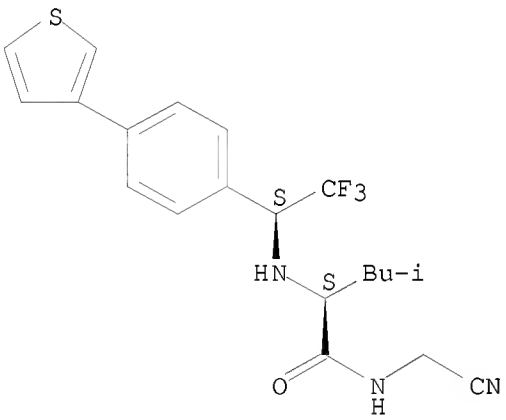
RN 603139-57-7 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,3,3,3-pentafluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]propyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



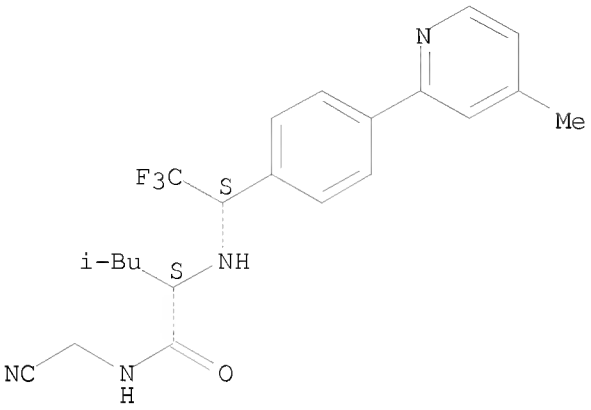
RN 603139-61-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(3-thienyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



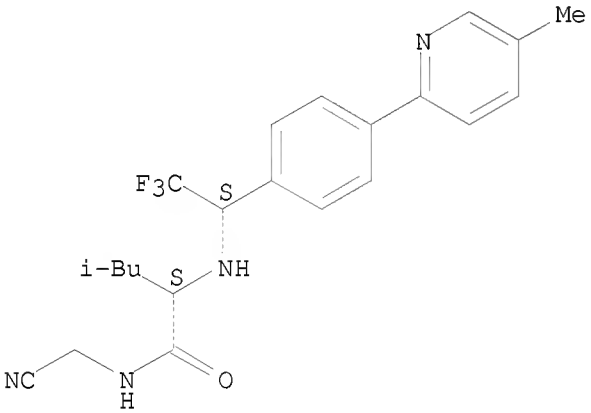
RN 603139-62-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(4-methyl-2-pyridinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



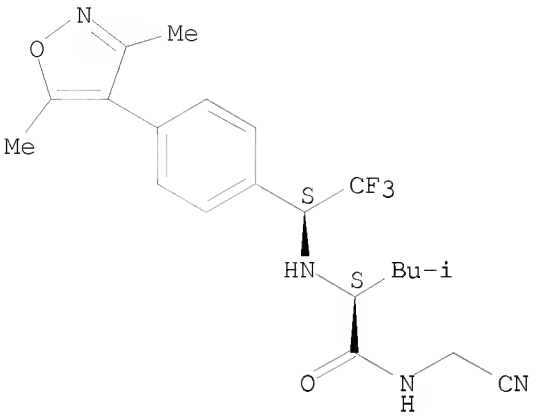
RN 603139-63-5 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(5-methyl-2-pyridinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



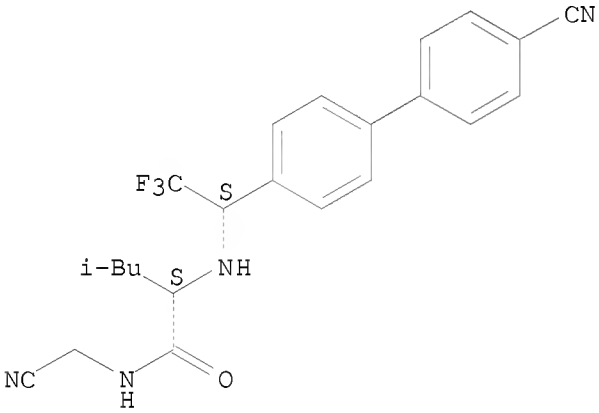
RN 603139-64-6 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[(1S)-1-[4-(3,5-dimethyl-4-isoxazolyl)phenyl]-2,2,2-trifluoroethyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



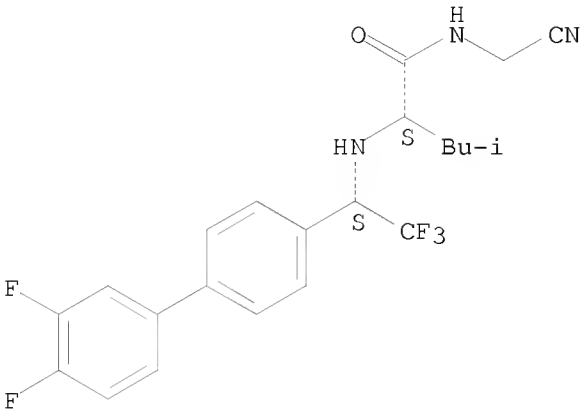
RN 603139-65-7 CAPLUS
CN Pentanamide, 2-[[(1S)-1-(4'-cyano[1,1'-biphenyl]-4-yl)-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

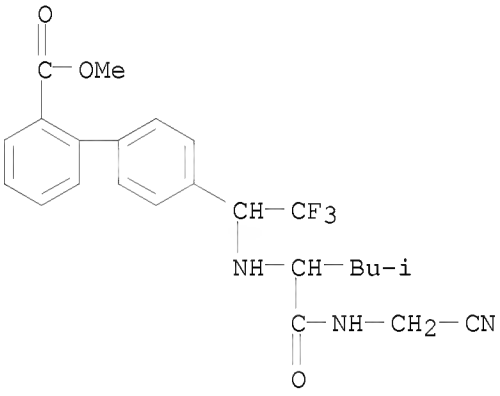


RN 603139-66-8 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[(1S)-1-(3',4'-difluoro[1,1'-biphenyl]-4-yl)-2,2,2-trifluoroethyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

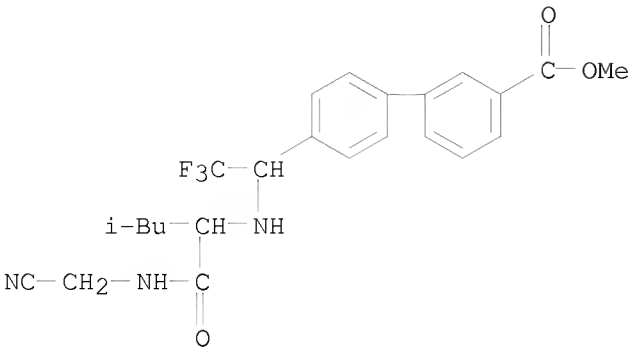
Absolute stereochemistry.



RN 603139-67-9 CAPLUS
CN [1,1'-Biphenyl]-2-carboxylic acid, 4'-[1-[[1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]-2,2,2-trifluoroethyl]-, methyl ester (CA INDEX NAME)

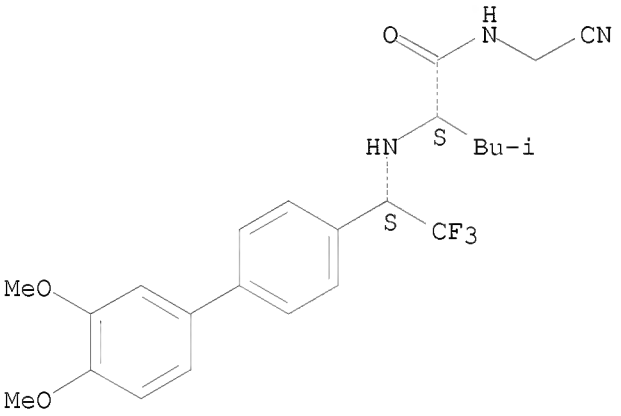


RN 603139-68-0 CAPLUS
CN [1,1'-Biphenyl]-3-carboxylic acid, 4'-[1-[[1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]-2,2,2-trifluoroethyl]-, methyl ester (CA INDEX NAME)



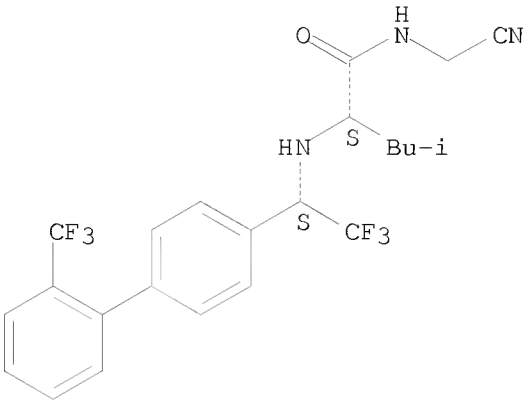
RN 603139-69-1 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[(1S)-1-(3',4'-dimethoxy[1,1'-biphenyl]-4-yl)-2,2,2-trifluoroethyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



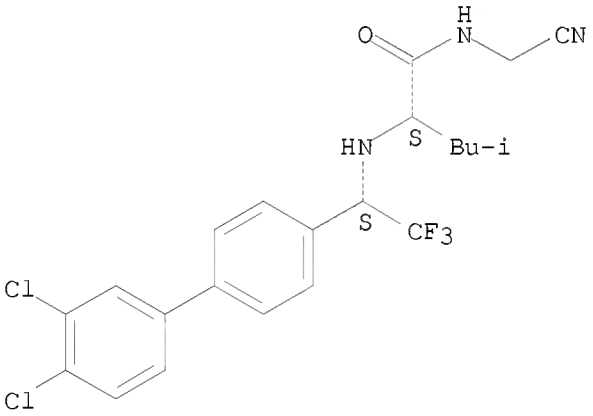
RN 603139-70-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[2'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



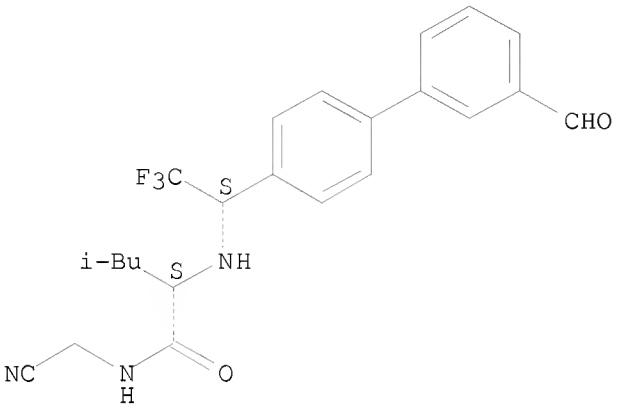
RN 603139-71-5 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[(1S)-1-(3',4'-dichloro[1,1'-biphenyl]-4-yl)-2,2,2-trifluoroethyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



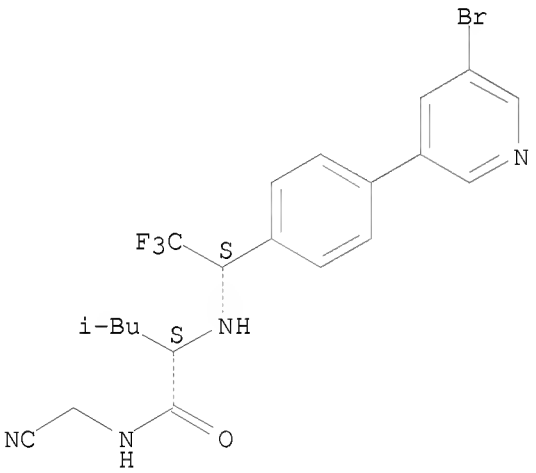
RN 603139-72-6 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-(3'-formyl[1,1'-biphenyl]-4-yl)ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



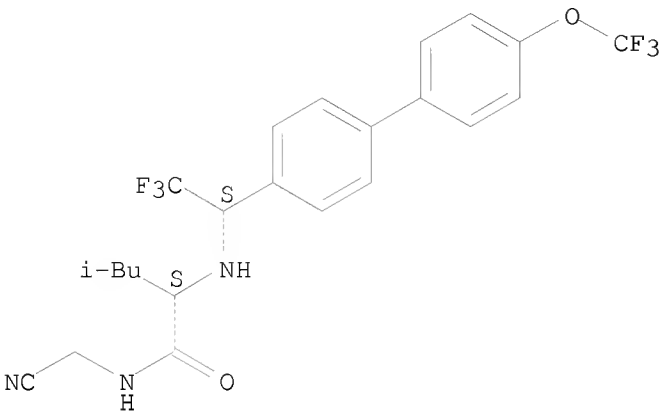
RN 603139-73-7 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4-(5-bromo-3-pyridinyl)phenyl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



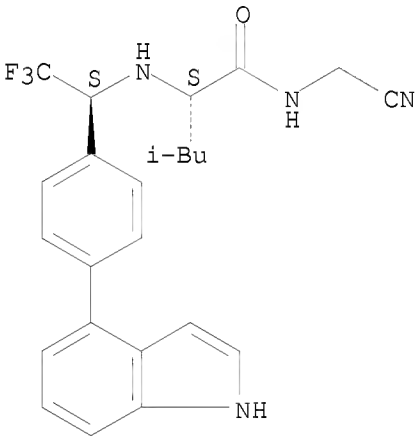
RN 603139-74-8 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(trifluoromethoxy)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



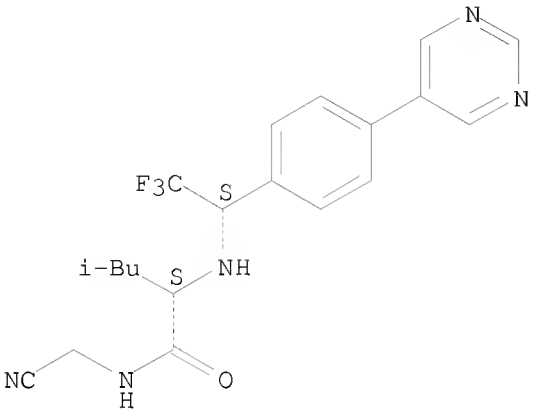
RN 603139-75-9 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(1H-indol-4-yl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



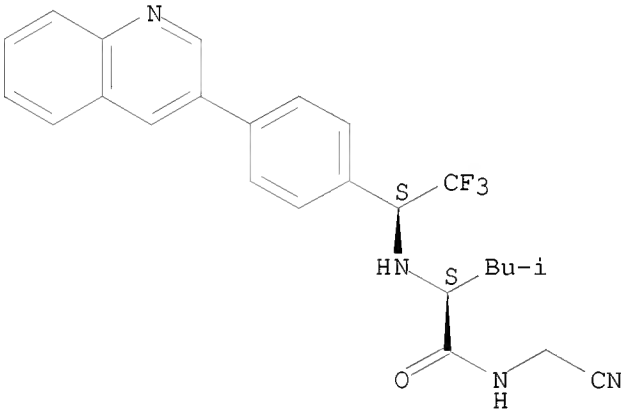
RN 603139-76-0 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(5-pyrimidinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

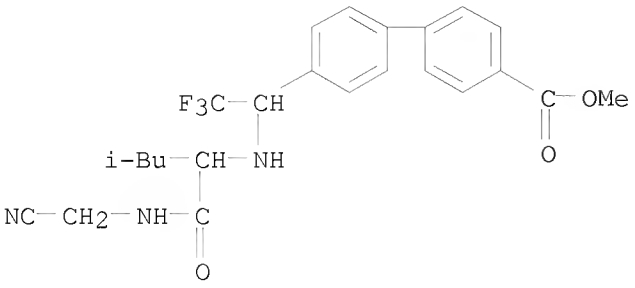


RN 603139-77-1 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(3-quinolinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

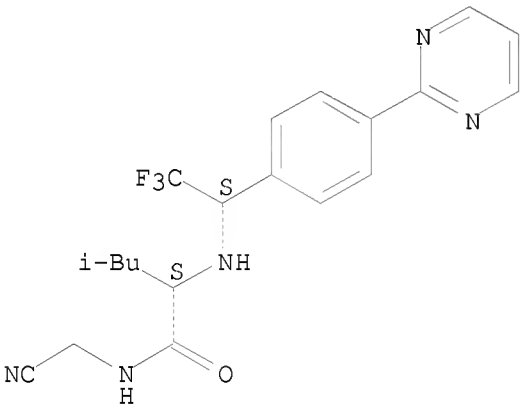


RN 603139-78-2 CAPLUS
CN [1,1'-Biphenyl]-4-carboxylic acid, 4'-[1-[[1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]-2,2,2-trifluoroethyl]-, methyl ester (CA INDEX NAME)



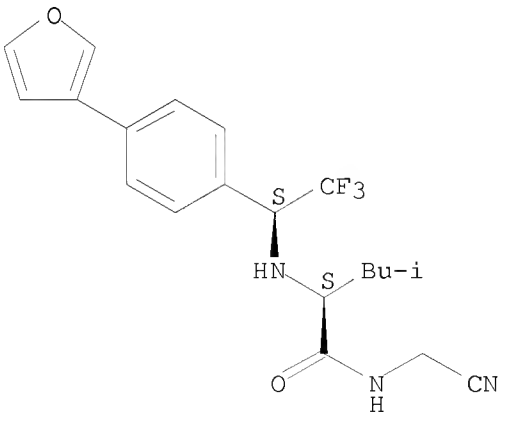
RN 603139-79-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(2-pyrimidinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



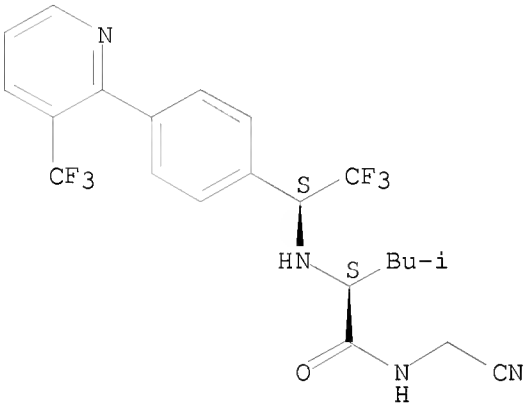
RN 603139-80-6 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(3-furanyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



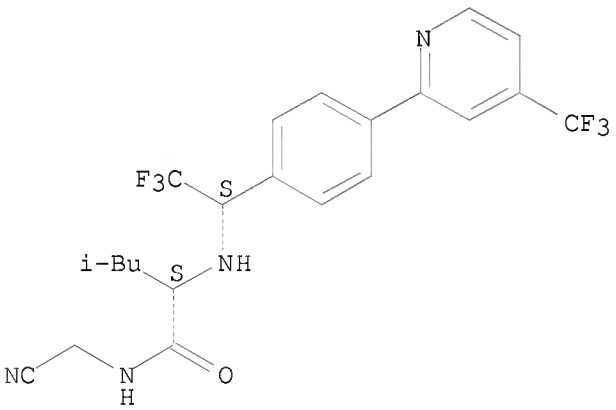
RN 603139-81-7 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-[3-(trifluoromethyl)-2-pyridinyl]phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



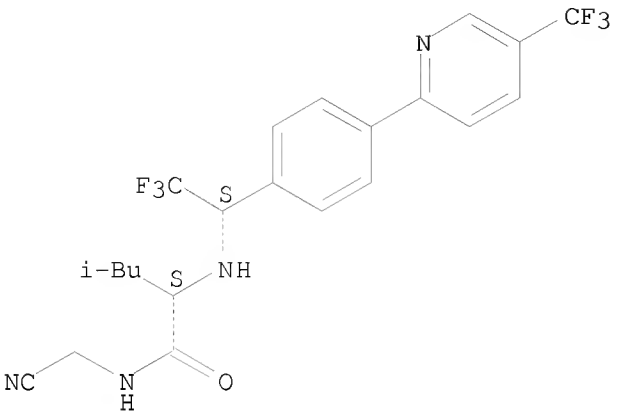
RN 603139-82-8 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-[4-(trifluoromethyl)-2-pyridinyl]phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



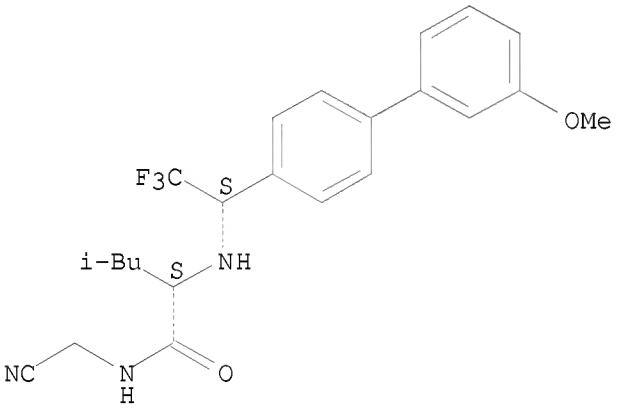
RN 603139-83-9 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-[5-(trifluoromethyl)-2-pyridinyl]phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



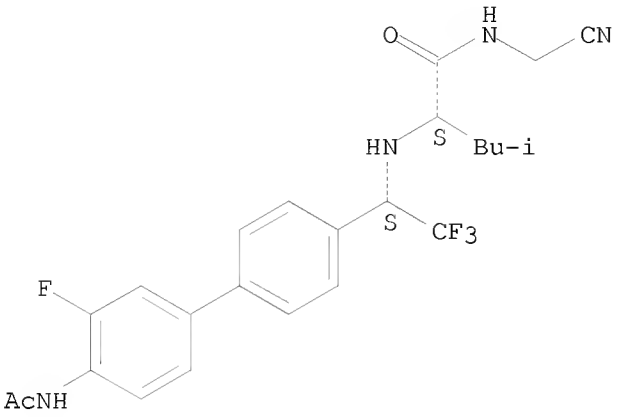
RN 603139-84-0 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-(3'-methoxy[1,1'-biphenyl]-4-yl)ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



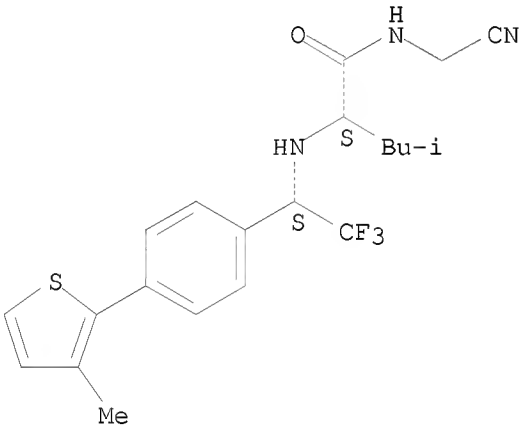
RN 603139-85-1 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4'-(acetylamino)-3'-fluoro[1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



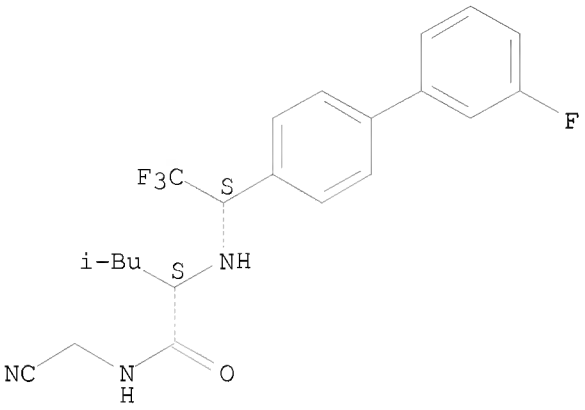
RN 603139-86-2 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(3-methyl-2-thienyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



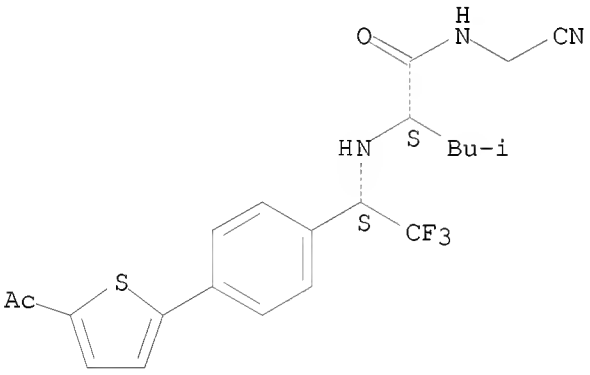
RN 603139-87-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-(3'-fluoro[1,1'-biphenyl]-4-yl)ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



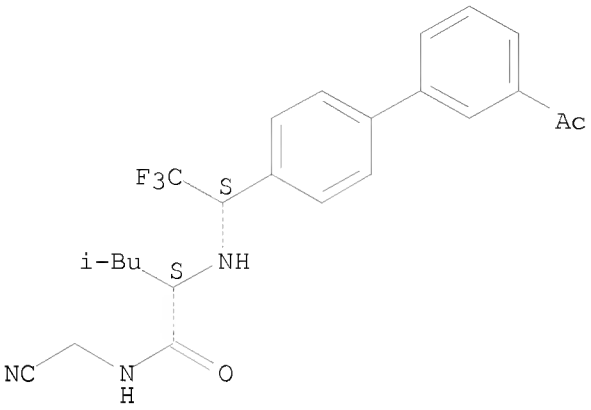
RN 603139-88-4 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4-(5-acetyl-2-thienyl)phenyl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



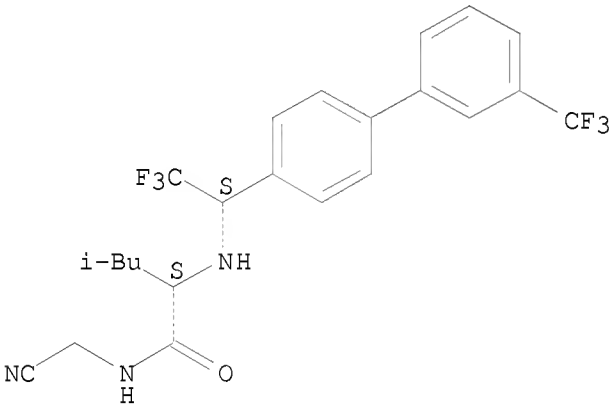
RN 603139-89-5 CAPLUS
CN Pentanamide, 2-[[(1S)-1-(3'-acetyl[1,1'-biphenyl]-4-yl)-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



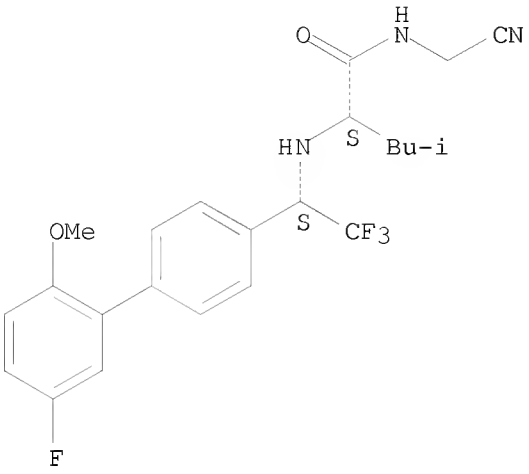
RN 603139-90-8 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[3'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



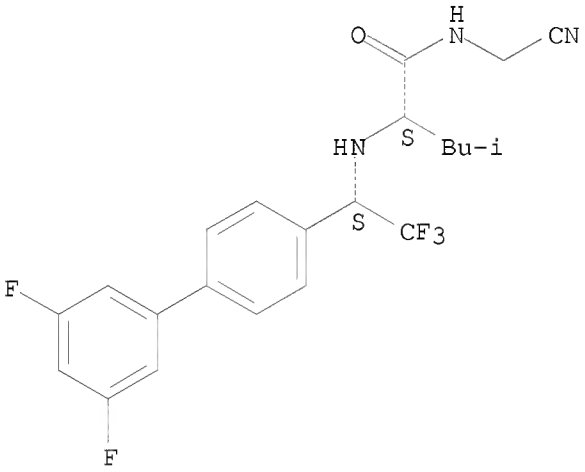
RN 603139-91-9 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-(5'-fluoro-2'-methoxy[1,1'-biphenyl]-4-yl)ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



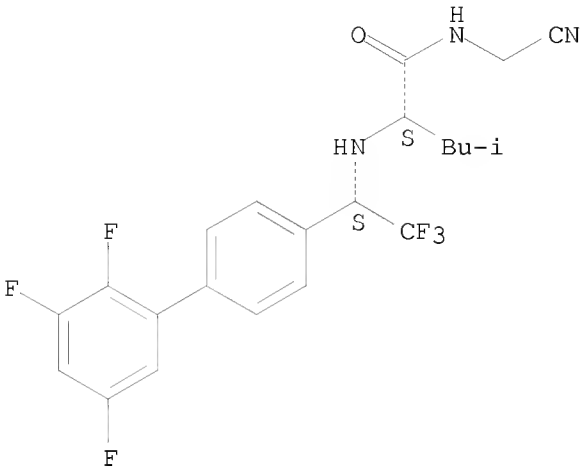
RN 603139-92-0 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[(1S)-1-(3',5'-difluoro[1,1'-biphenyl]-4-yl)-2,2,2-trifluoroethyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

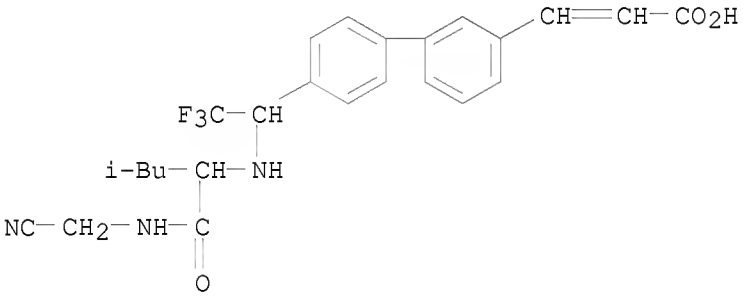


RN 603139-93-1 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-(2',3',5'-trifluoro[1,1'-biphenyl]-4-yl)ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

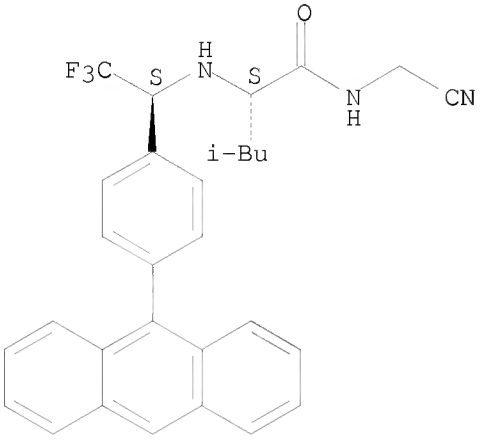


RN 603139-94-2 CAPLUS
CN 2-Propenoic acid, 3-[4'-[1-[[1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]-2,2,2-trifluoroethyl][1,1'-biphenyl]-3-yl]- (CA INDEX NAME)



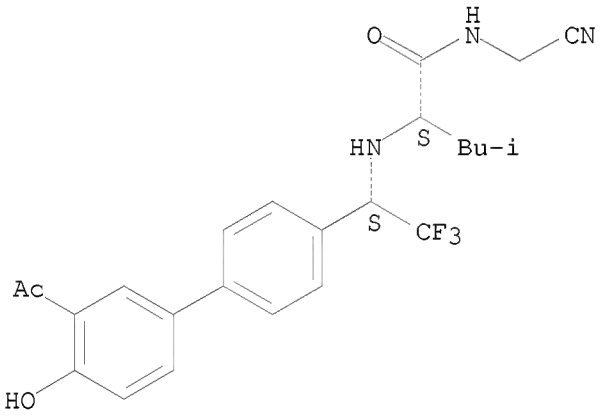
RN 603139-95-3 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4-(9-anthracenyl)phenyl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



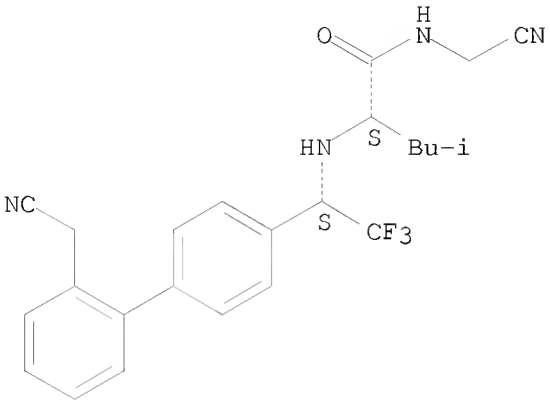
RN 603139-97-5 CAPLUS
CN Pentanamide, 2-[[(1S)-1-(3'-acetyl-4'-hydroxy[1,1'-biphenyl]-4-yl)-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



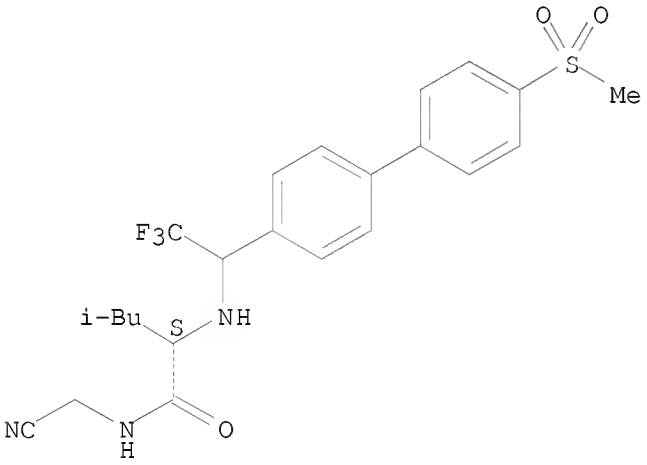
RN 603139-98-6 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[(1S)-1-[2'-(cyanomethyl)[1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



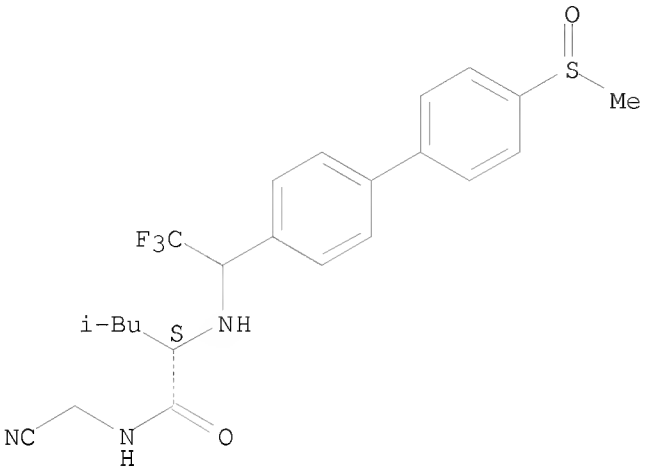
RN 603139-99-7 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



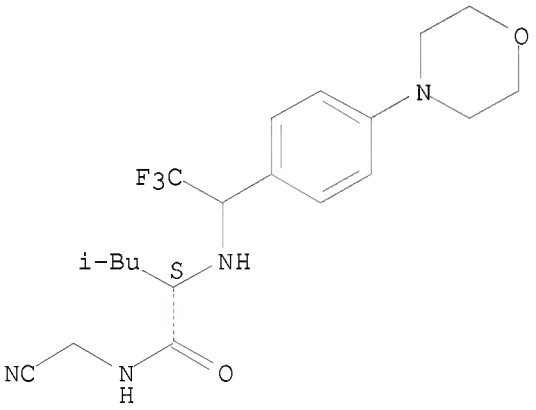
RN 603140-00-7 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4'-(methylsulfinyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



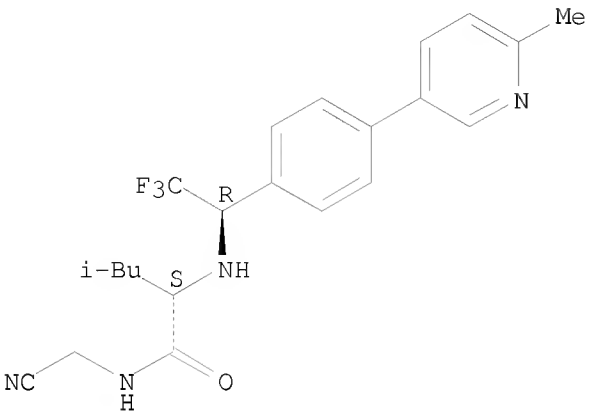
RN 603140-01-8 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4-(4-morpholinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



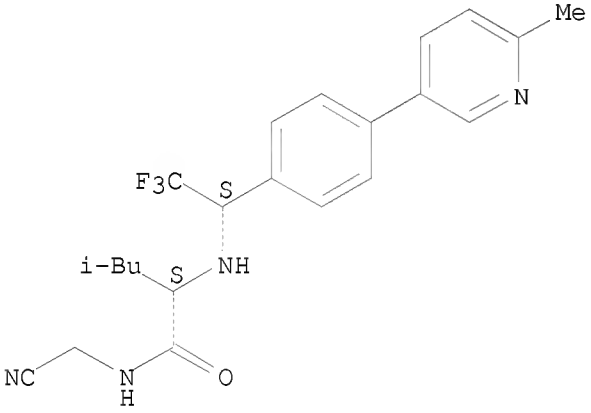
RN 603140-02-9 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1R)-2,2,2-trifluoro-1-[4-(6-methyl-3-pyridinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



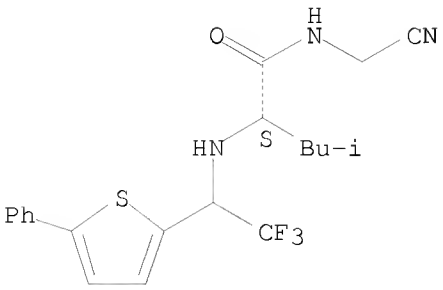
RN 603140-03-0 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(6-methyl-3-pyridinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



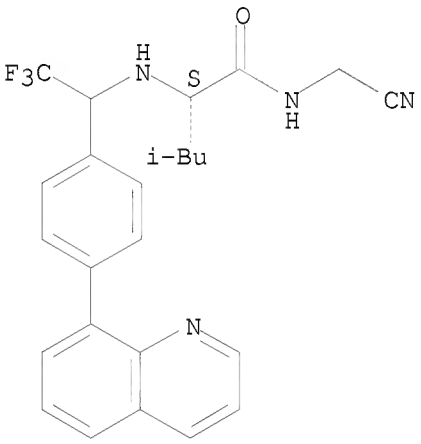
RN 603140-04-1 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-(5-phenyl-2-thienyl)ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



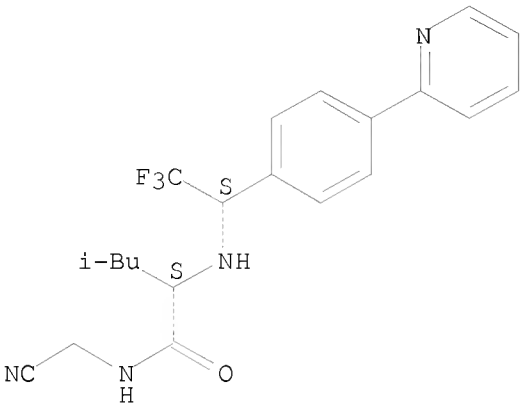
RN 603140-05-2 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4-(8-quinolinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



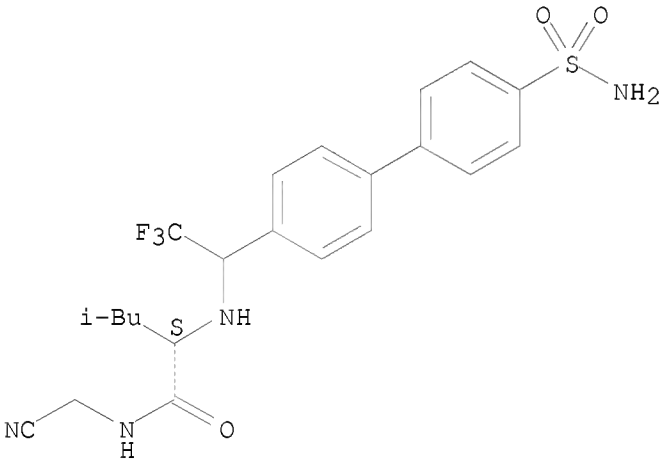
RN 603140-06-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(2-pyridinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



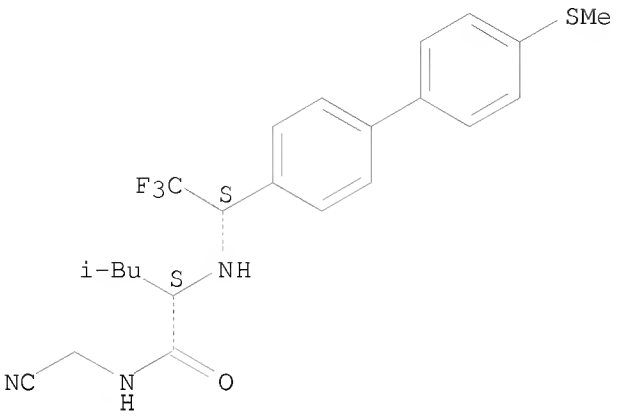
RN 603140-07-4 CAPLUS
CN Pentanamide, 2-[[1-[4'-(aminosulfonyl)[1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



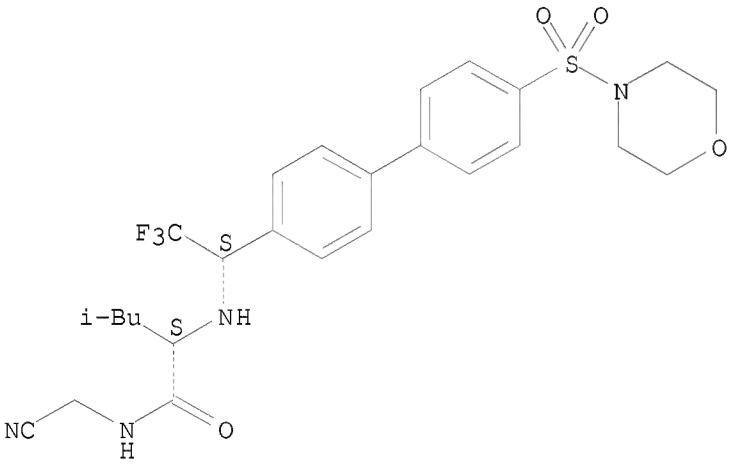
RN 603140-08-5 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylthio)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



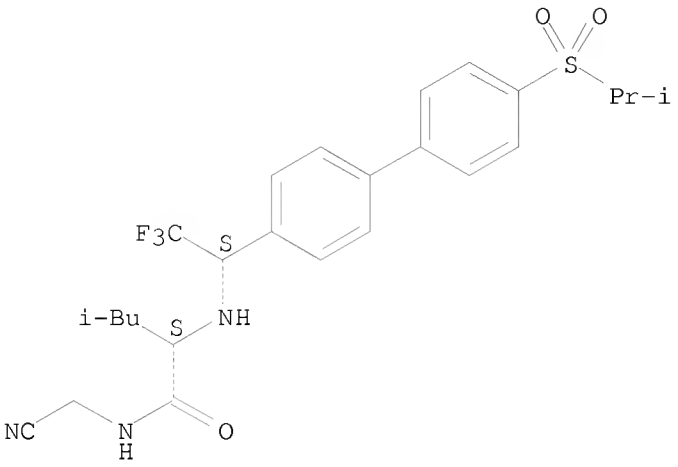
RN 603140-10-9 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(4-morpholinylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



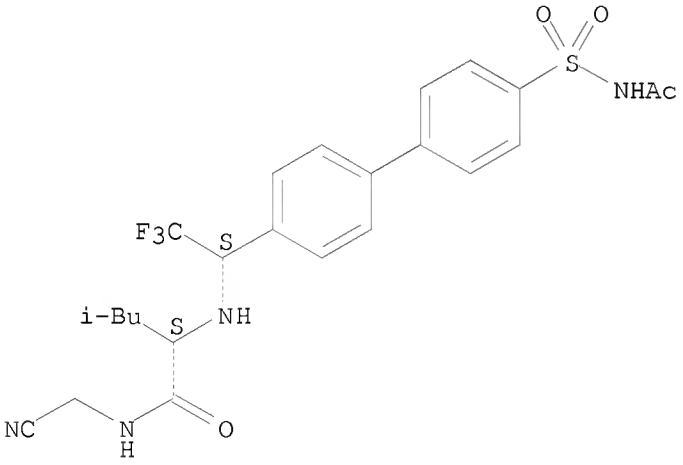
RN 603140-11-0 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-[(1-methylethyl)sulfonyl][1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



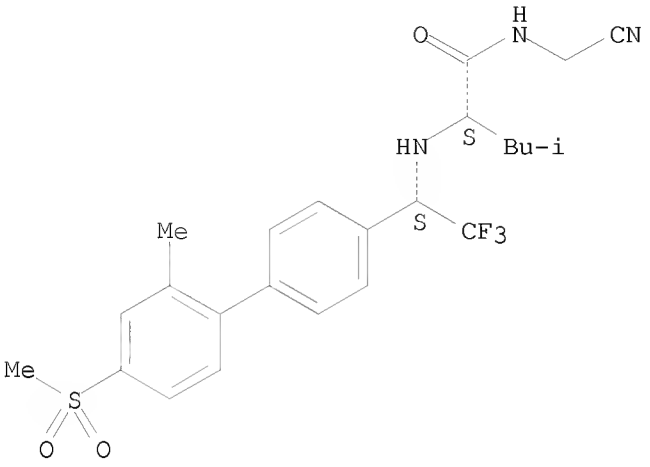
RN 603140-12-1 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4'-[(acetylamino)sulfonyl][1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

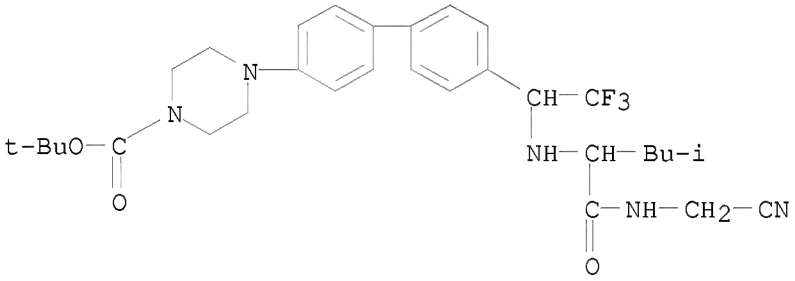


RN 603140-13-2 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[2'-methyl-4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

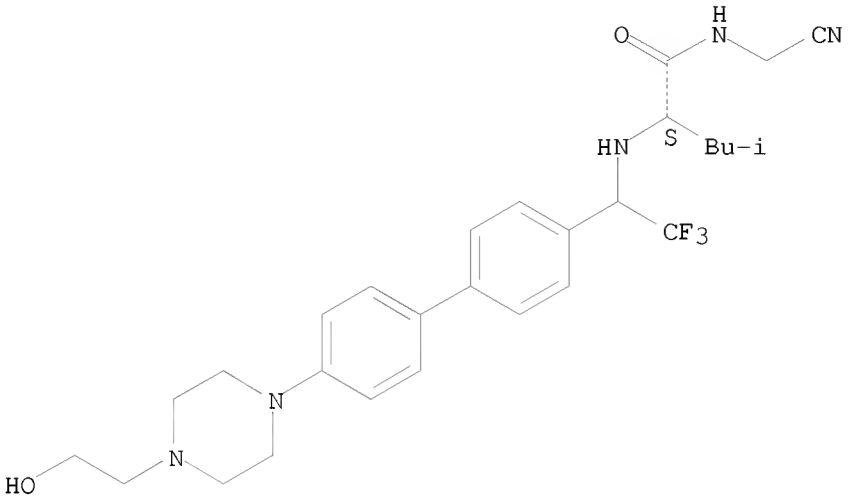


RN 603140-15-4 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4'-[1-[[1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]-2,2,2-trifluoroethyl][1,1'-biphenyl]-4-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



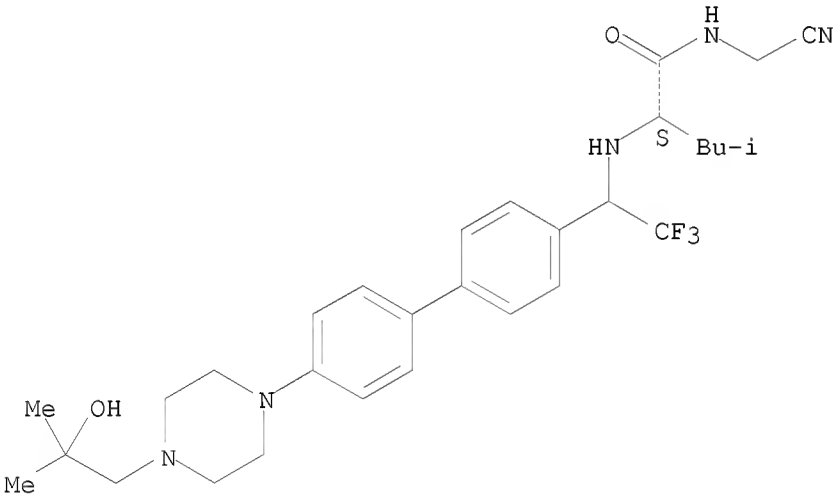
RN 603140-16-5 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4'-[4-(2-hydroxyethyl)-1-piperazinyl][1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



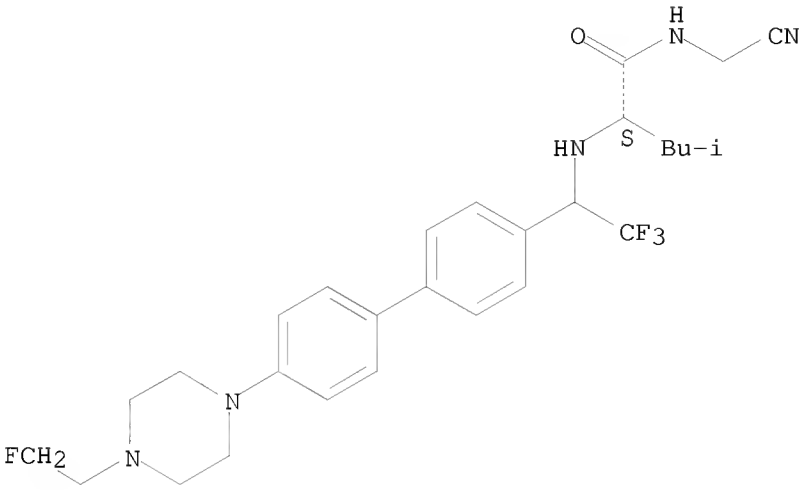
RN 603140-17-6 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4'-[4-(2-hydroxy-2-methylpropyl)-1-piperazinyl][1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



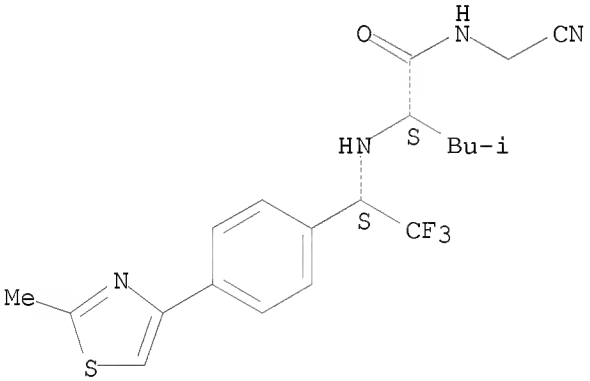
RN 603140-21-2 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4'-[4-(2-fluoroethyl)-1-piperazinyl][1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



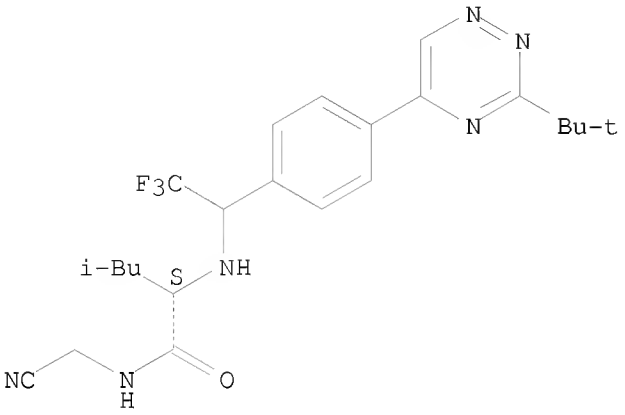
RN 603140-24-5 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(2-methyl-4-thiazolyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



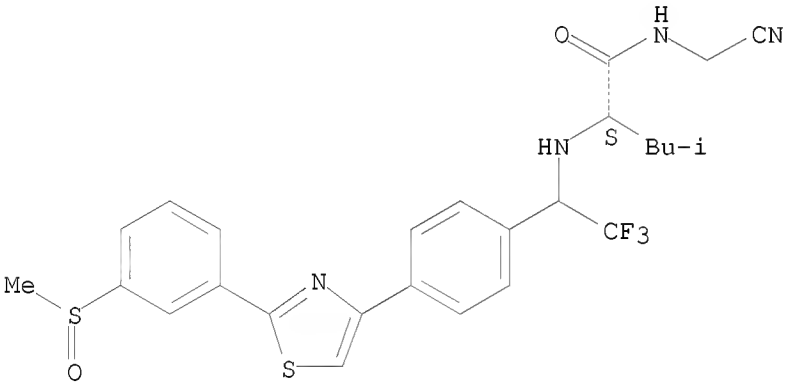
RN 603140-25-6 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[1-[4-[3-(1,1-dimethylethyl)-1,2,4-triazin-5-yl]phenyl]-2,2,2-trifluoroethyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



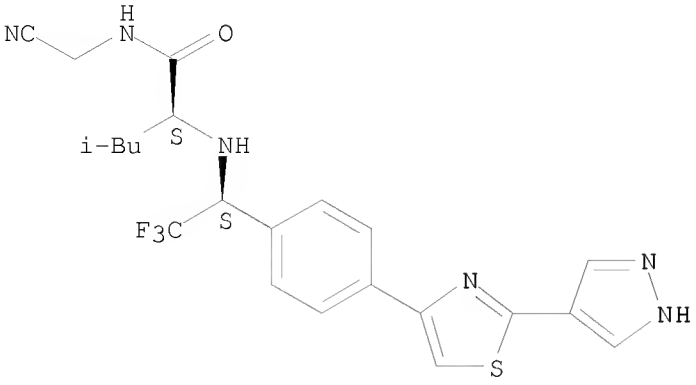
RN 603140-26-7 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4-[2-[3-(methylsulfinyl)phenyl]-4-thiazolyl]phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



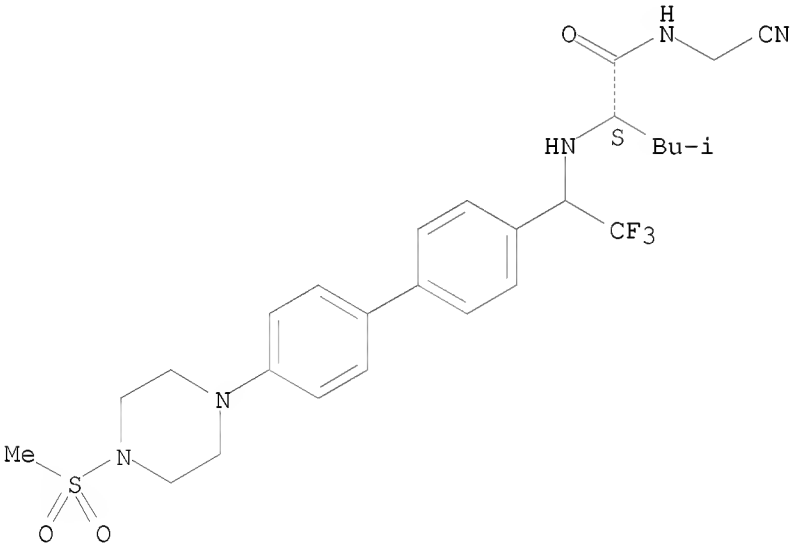
RN 603140-27-8 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-[2-(1H-pyrazol-4-yl)-4-thiazolyl]phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



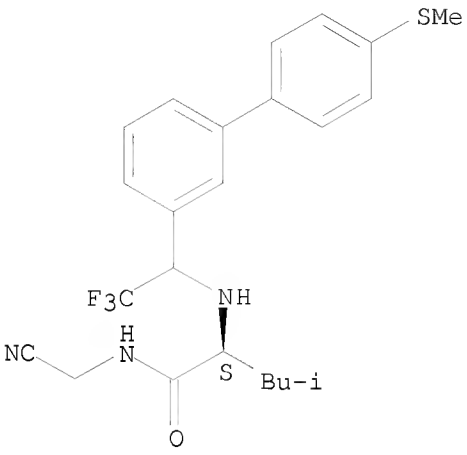
RN 603140-28-9 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4'-[4-(methylsulfonyl)-1-piperazinyl][1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)-(CA INDEX NAME)

Absolute stereochemistry.



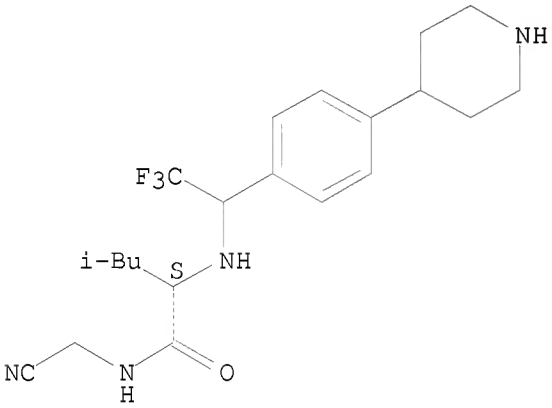
RN 603140-30-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4'-(methylthio)[1,1'-biphenyl]-3-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



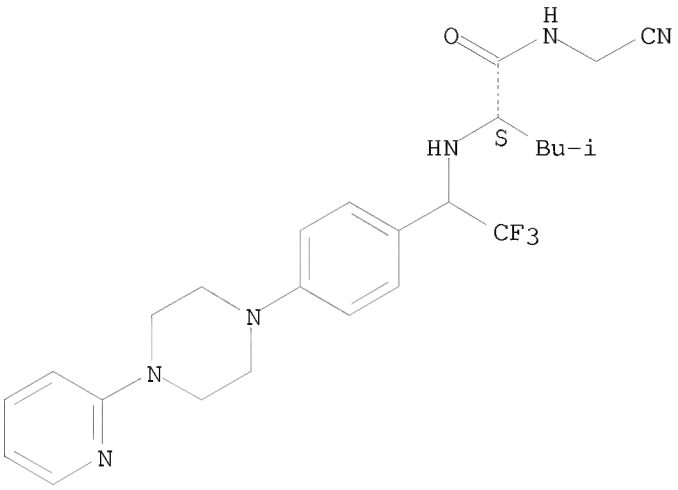
RN 603140-34-7 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4-(4-piperidinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

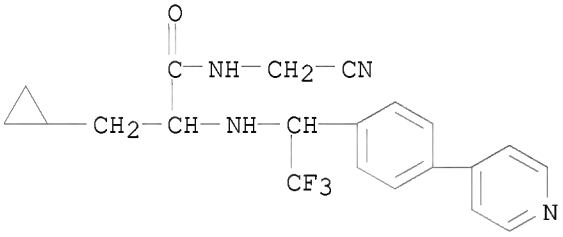


RN 603140-35-8 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4-[4-(2-pyridinyl)-1-piperazinyl]phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

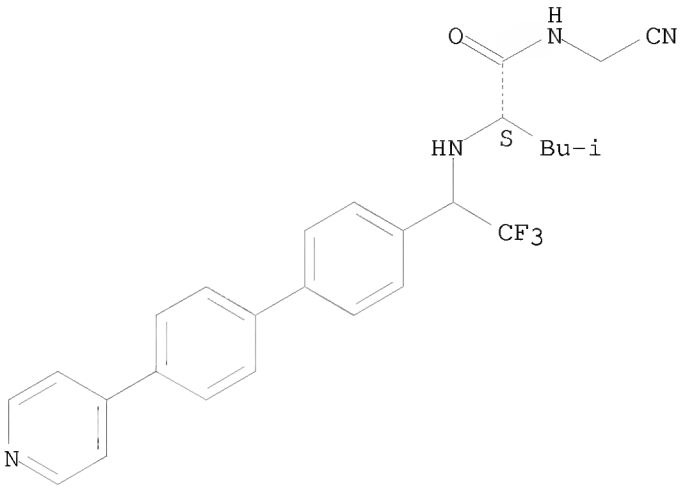


RN 603140-37-0 CAPLUS
CN Cyclopropanepropanamide, N-(cyanomethyl)-α-[[2,2,2-trifluoro-1-[4-(4-pyridinyl)phenyl]ethyl]amino]- (CA INDEX NAME)



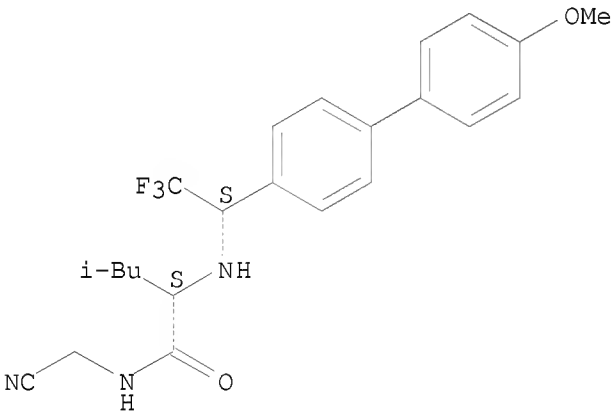
RN 603140-38-1 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4'-(4-pyridinyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



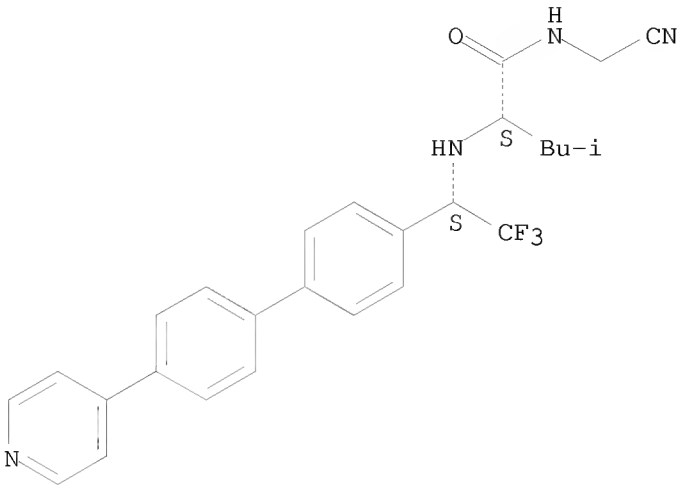
RN 603140-40-5 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-(4'-methoxy[1,1'-biphenyl]-4-yl)ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



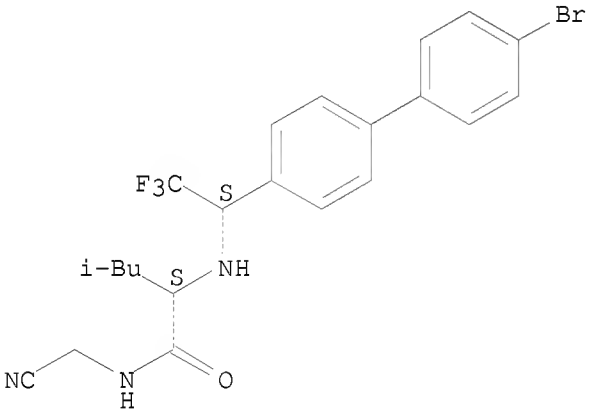
RN 603140-42-7 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(4-pyridinyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



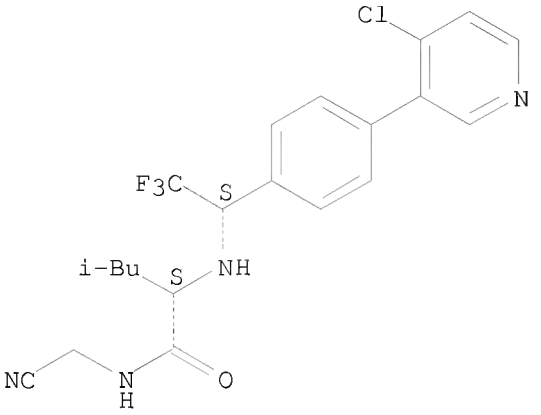
RN 603140-44-9 CAPLUS
CN Pentanamide, 2-[[(1S)-1-(4'-bromo[1,1'-biphenyl]-4-yl)-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



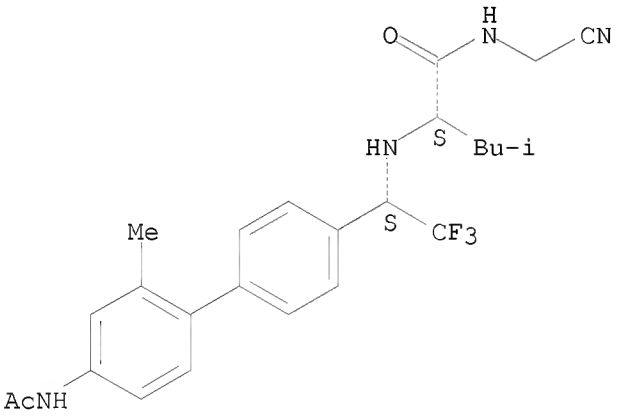
RN 603140-45-0 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4-(4-chloro-3-pyridinyl)phenyl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



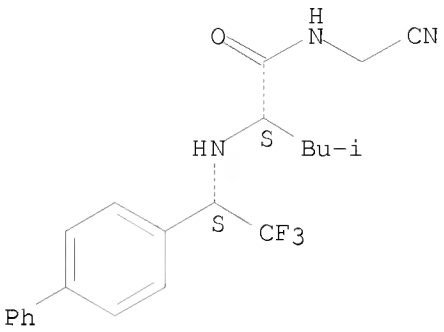
RN 603140-46-1 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4'-(acetylamino)-2'-methyl[1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



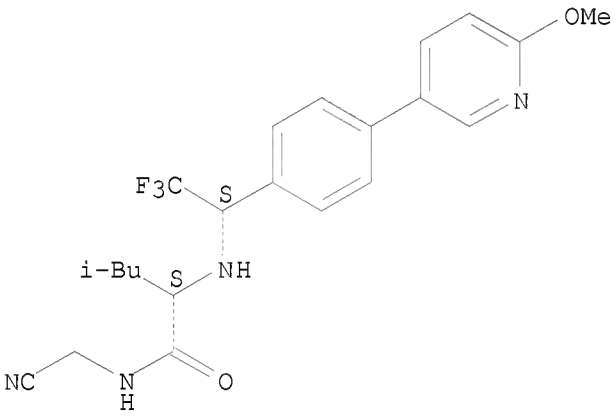
RN 603140-47-2 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[1,1'-biphenyl]-4-yl-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



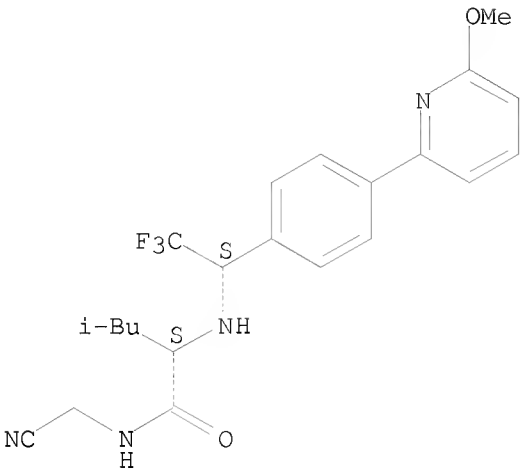
RN 603140-48-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(6-methoxy-3-pyridinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



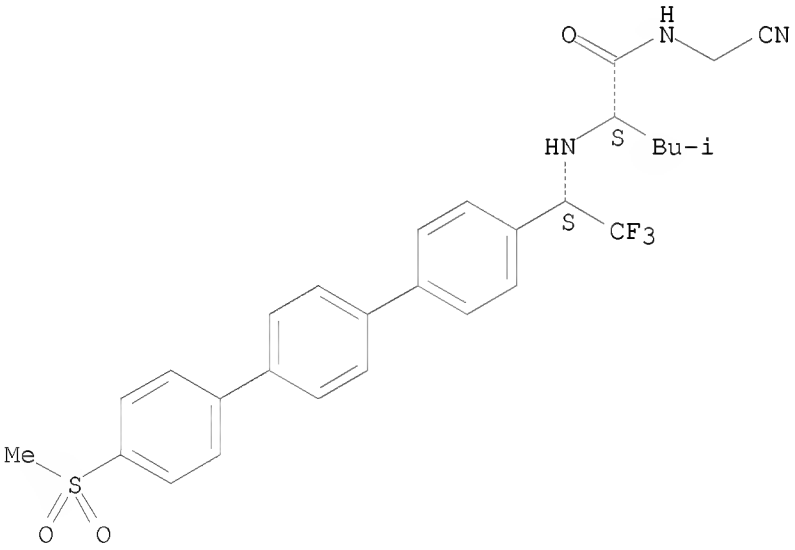
RN 603140-49-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(6-methoxy-2-pyridinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

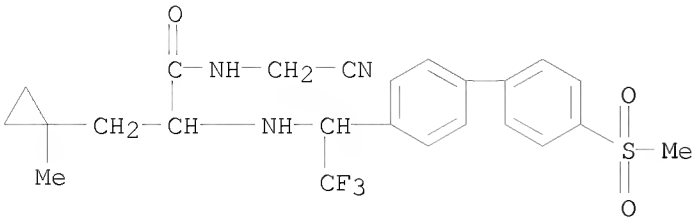


RN 603140-50-7 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4''-(methylsulfonyl)[1,1':4',1''-terphenyl]-4-yl]ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

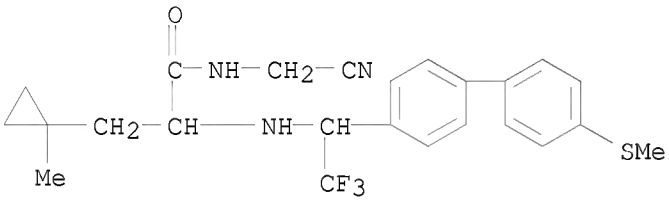
Absolute stereochemistry.



RN 603140-52-9 CAPLUS
CN Cyclopropanepropanamide, N-(cyanomethyl)-1-methyl-α-[[2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]- (CA INDEX NAME)

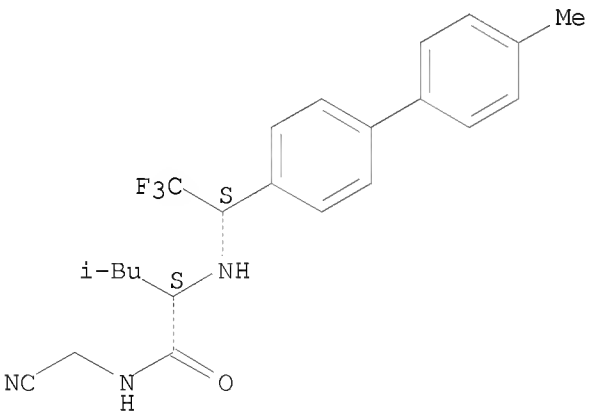


RN 603140-53-0 CAPLUS
CN Cyclopropanepropanamide, N-(cyanomethyl)-1-methyl-α-[[2,2,2-trifluoro-1-[4'-(methylthio)[1,1'-biphenyl]-4-yl]ethyl]amino]- (CA INDEX NAME)



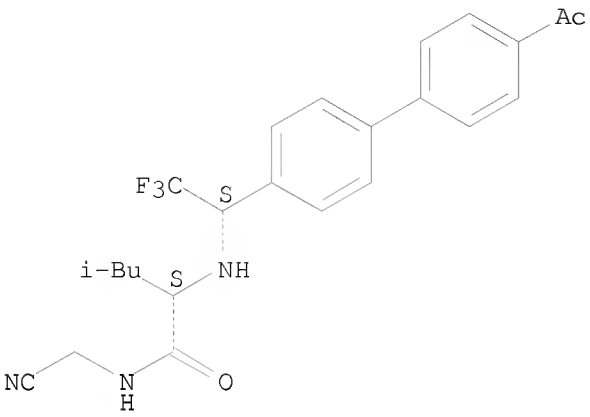
RN 603140-54-1 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-(4'-methyl[1,1'-biphenyl]-4-yl)ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



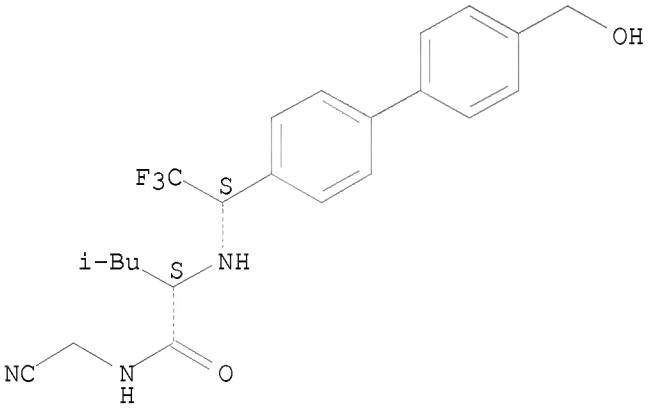
RN 603140-55-2 CAPLUS
CN Pentanamide, 2-[[(1S)-1-(4'-acetyl[1,1'-biphenyl]-4-yl)-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



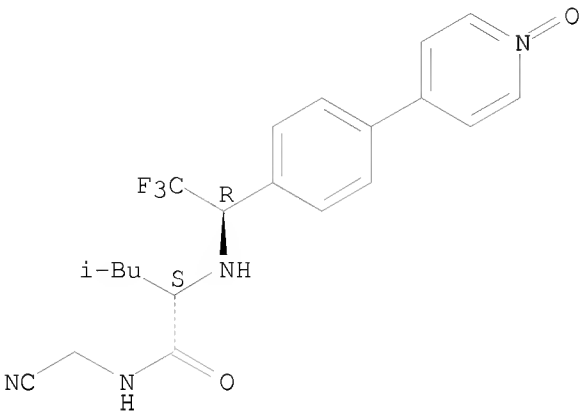
RN 603140-56-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(hydroxymethyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



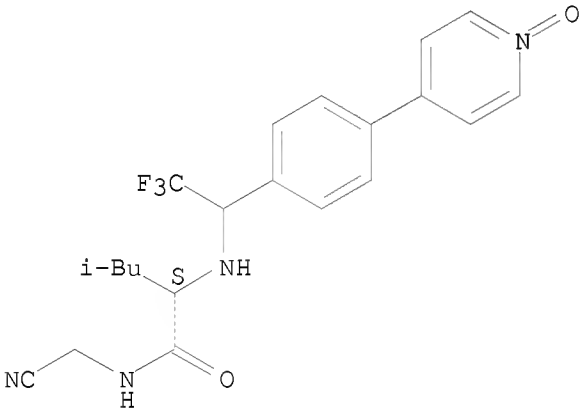
RN 603140-57-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1R)-2,2,2-trifluoro-1-[4-(1-oxido-4-pyridinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



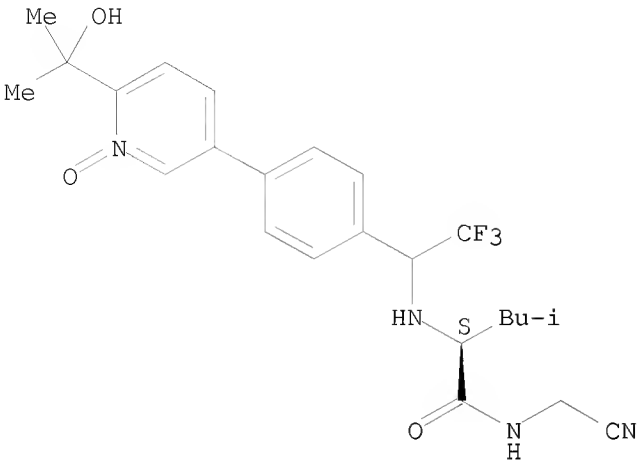
RN 603140-58-5 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4-(1-oxido-4-pyridinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



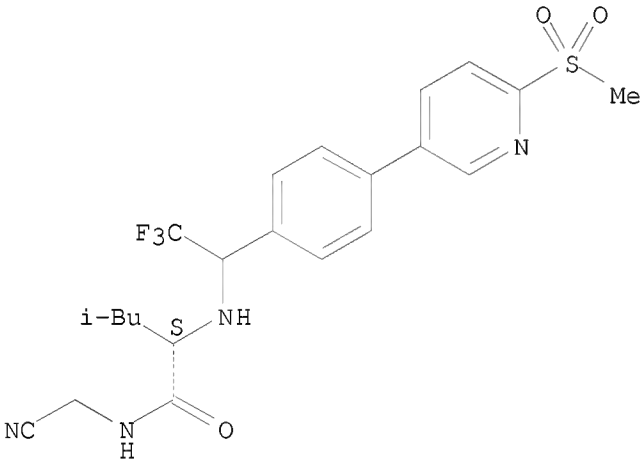
RN 603140-59-6 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4-[6-(1-hydroxy-1-methylethyl)-1-oxido-3-pyridinyl]phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



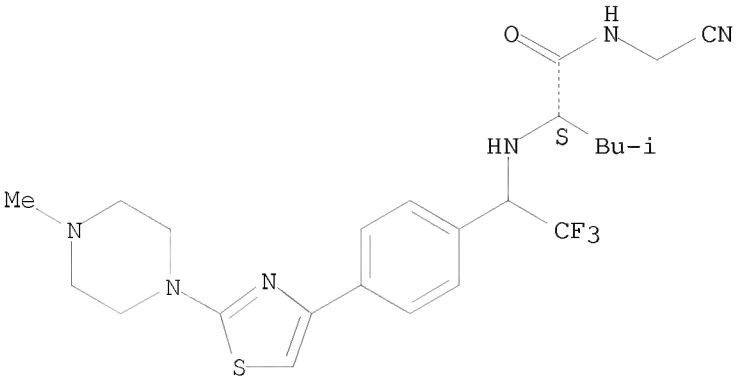
RN 603140-60-9 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4-[6-(methylsulfonyl)-3-pyridinyl]phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



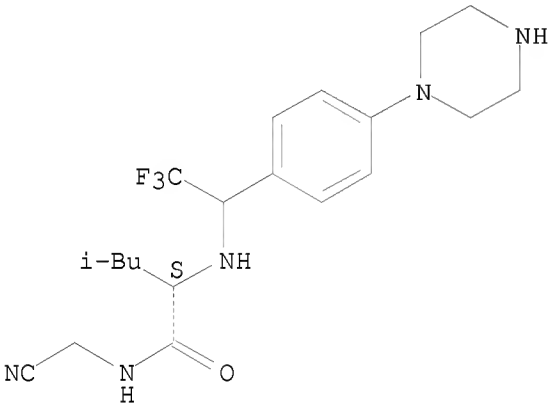
RN 603140-61-0 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4-[2-(4-methyl-1-piperazinyl)-4-thiazolyl]phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



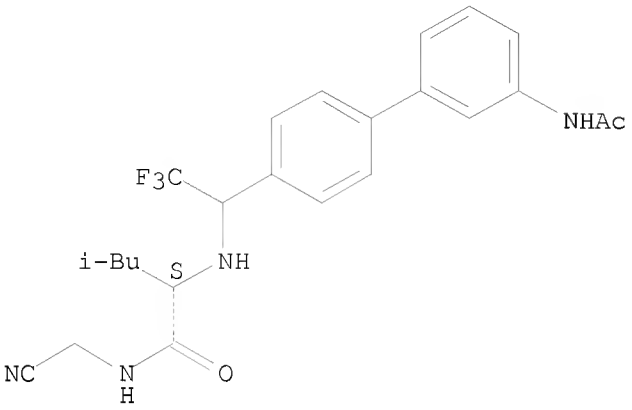
RN 603140-63-2 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4-(1-piperazinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



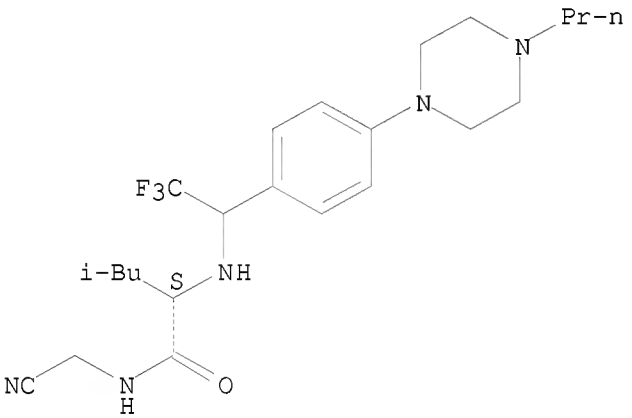
RN 603140-64-3 CAPLUS
CN Pentanamide, 2-[[1-[3'-(acetylamino)[1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



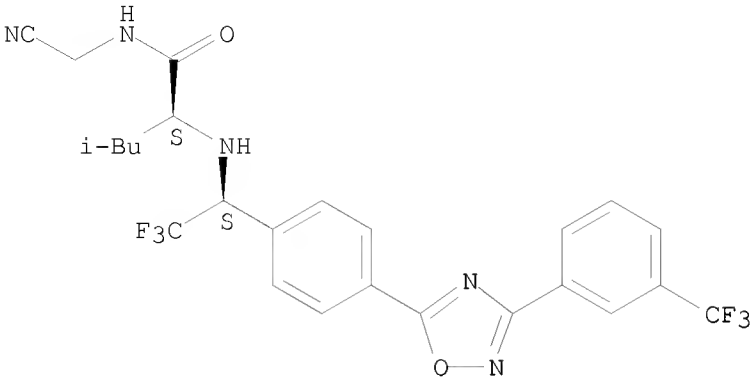
RN 603140-65-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4-(4-propyl-1-piperazinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



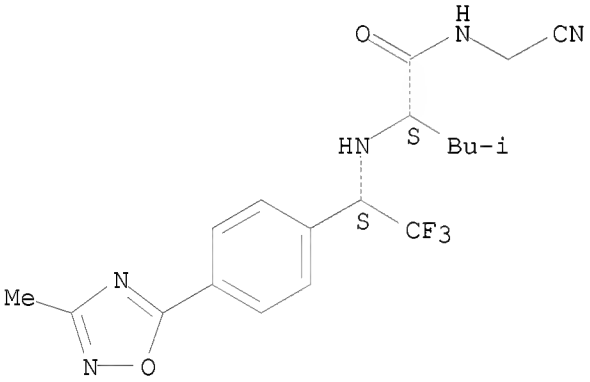
RN 603140-68-7 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-[3-[3-(trifluoromethyl)phenyl]-1,2,4-oxadiazol-5-yl]phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



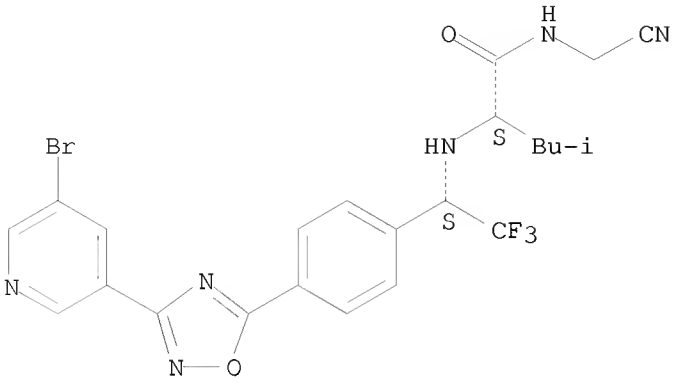
RN 603140-71-2 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(3-methyl-1,2,4-oxadiazol-5-yl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



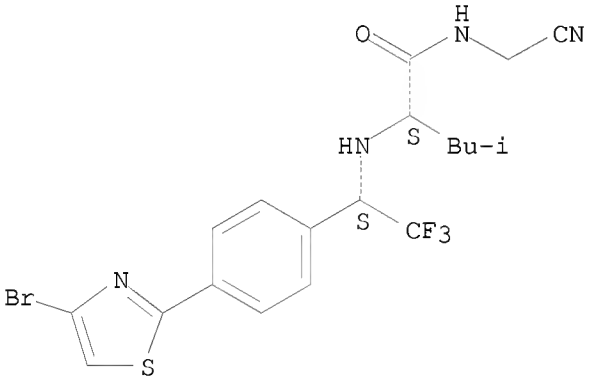
RN 603140-72-3 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4-[3-(5-bromo-3-pyridinyl)-1,2,4-oxadiazol-5-yl]phenyl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



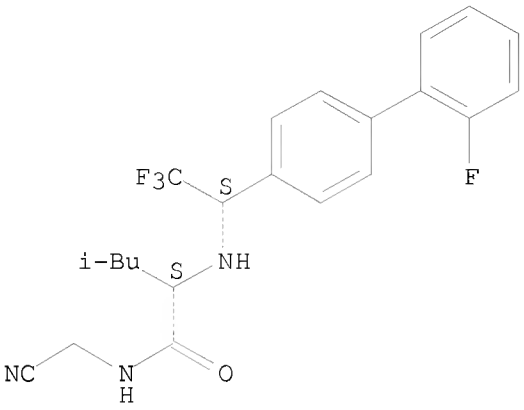
RN 603140-78-9 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4-(4-bromo-2-thiazolyl)phenyl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



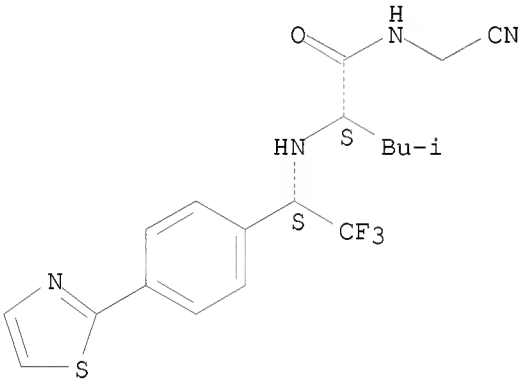
RN 603140-81-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-(2'-fluoro[1,1'-biphenyl]-4-yl)ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



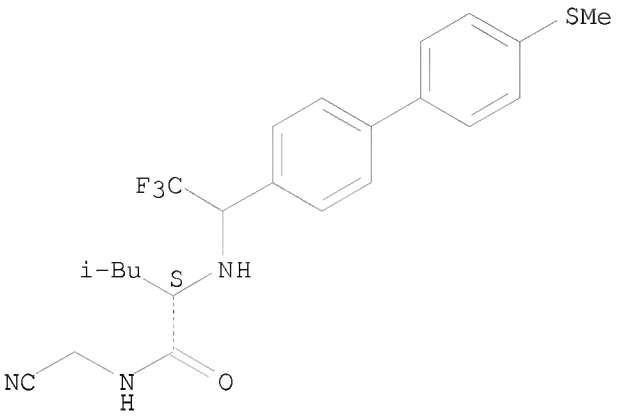
RN 603140-82-5 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(2-thiazolyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



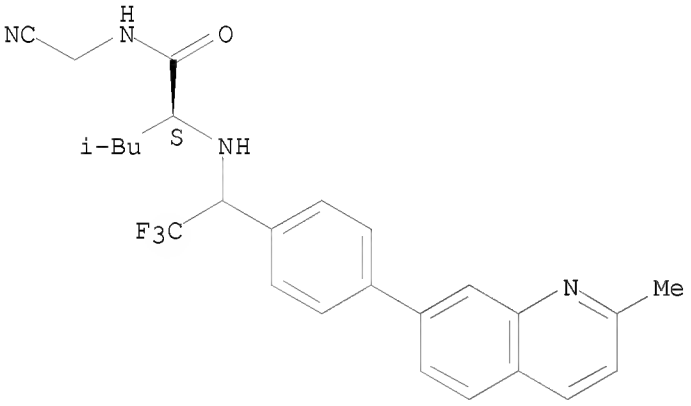
RN 603140-83-6 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4'-(methylthio)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



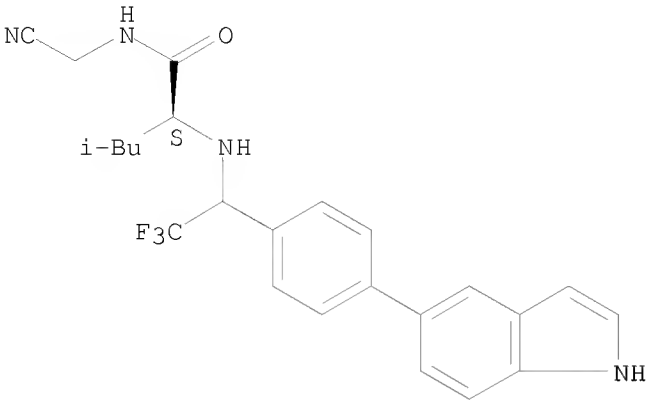
RN 603140-84-7 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4-(2-methyl-7-quinolinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



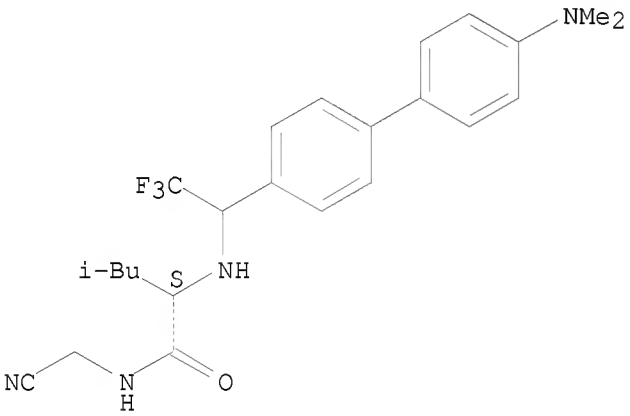
RN 603140-85-8 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4-(1H-indol-5-yl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



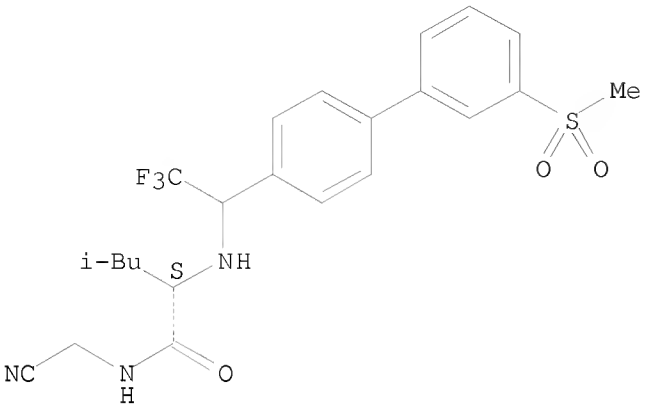
RN 603140-86-9 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[1-[4'-(dimethylamino)[1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

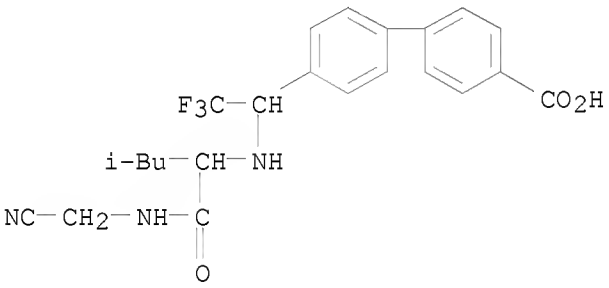


RN 603140-89-2 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[3'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

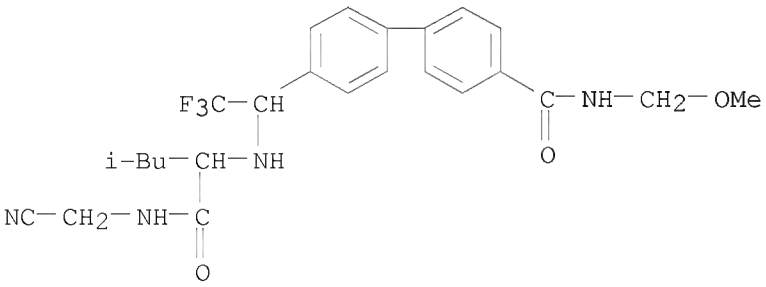
Absolute stereochemistry.



RN 603140-90-5 CAPLUS
CN [1,1'-Biphenyl]-4-carboxylic acid, 4'-[1-[[1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]-2,2,2-trifluoroethyl]- (CA INDEX NAME)

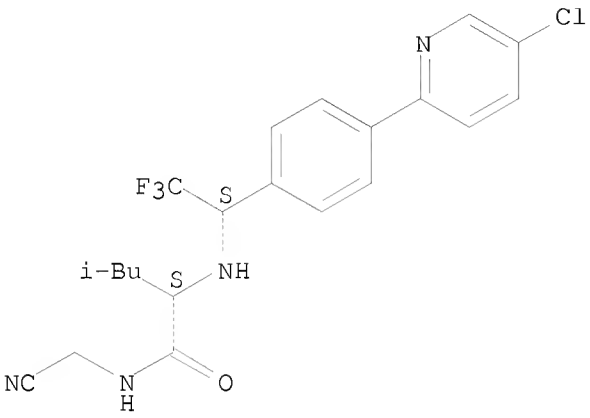


RN 603140-91-6 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, 4'-[1-[[1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]-2,2,2-trifluoroethyl]-N-(methoxymethyl)- (CA INDEX NAME)



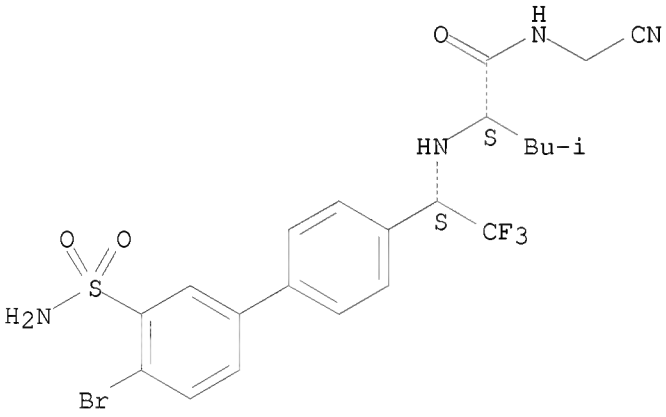
RN 603140-93-8 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4-(5-chloro-2-pyridinyl)phenyl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



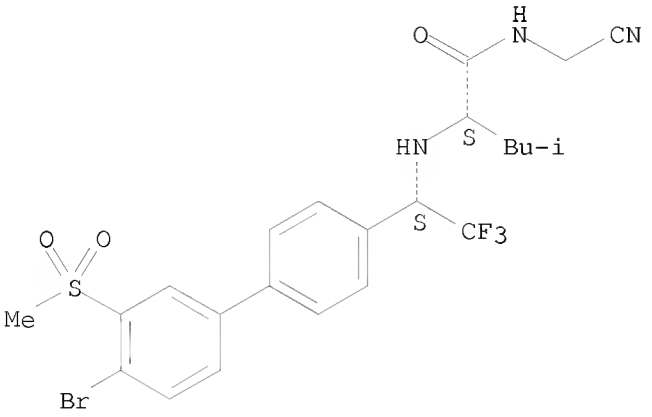
RN 603140-94-9 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[3'-(aminosulfonyl)-4'-bromo[1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



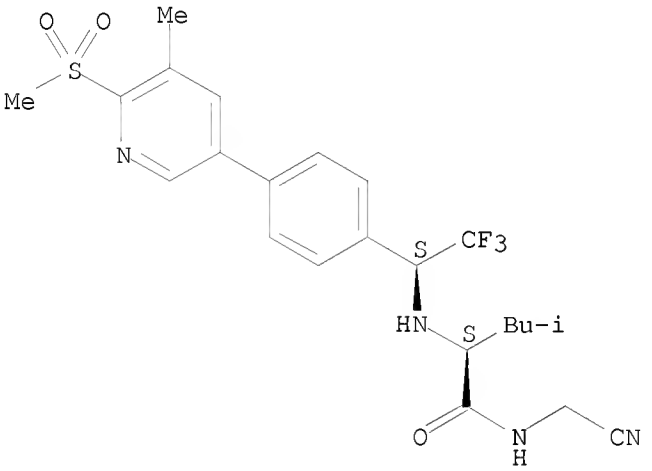
RN 603140-95-0 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4'-bromo-3'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



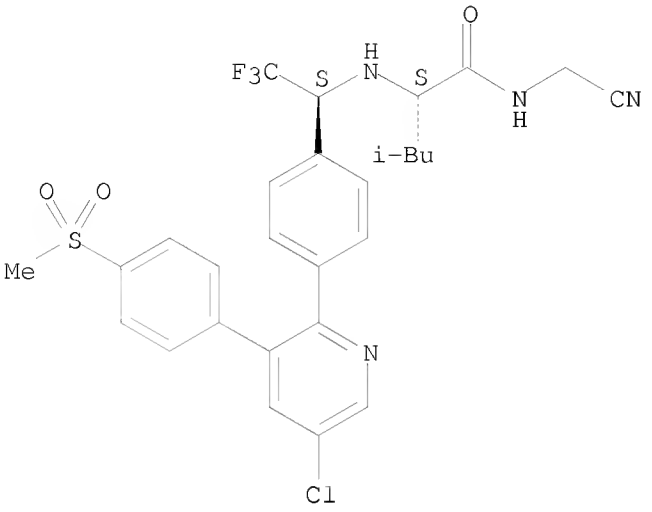
RN 603140-96-1 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-[5-methyl-6-(methylsulfonyl)-3-pyridinyl]phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



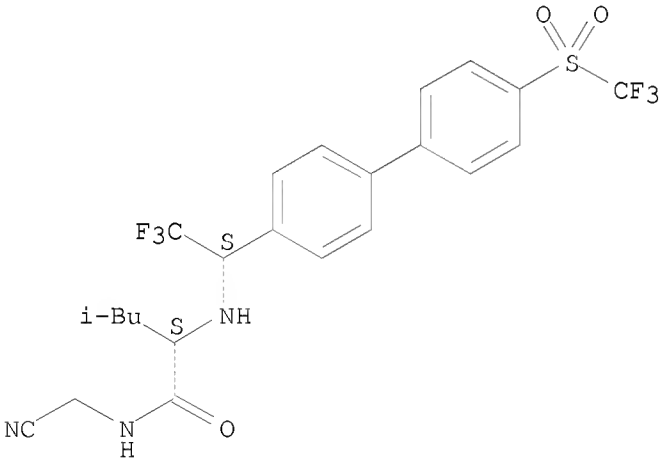
RN 603140-97-2 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4-[5-chloro-3-[4-(methylsulfonyl)phenyl]-2-pyridinyl]phenyl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



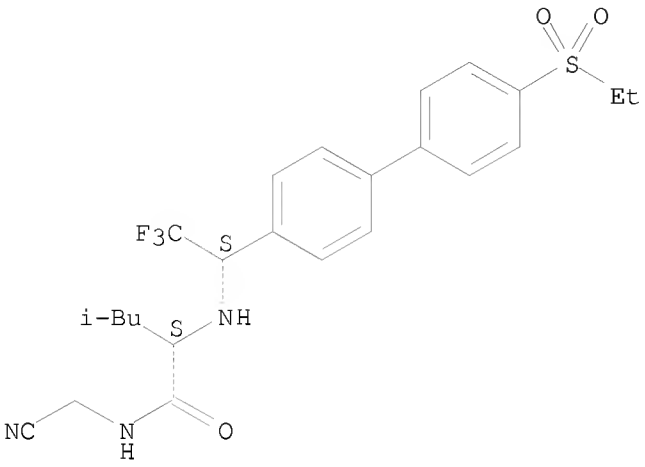
RN 603140-99-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-[(trifluoromethyl)sulfonyl][1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



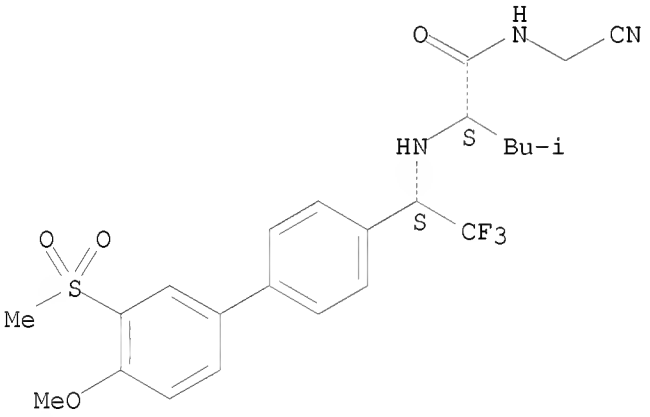
RN 603141-02-2 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[(1S)-1-[4'-(ethylsulfonyl)[1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



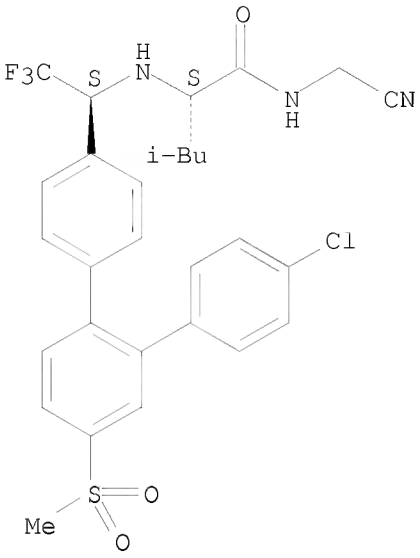
RN 603141-05-5 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-methoxy-3'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



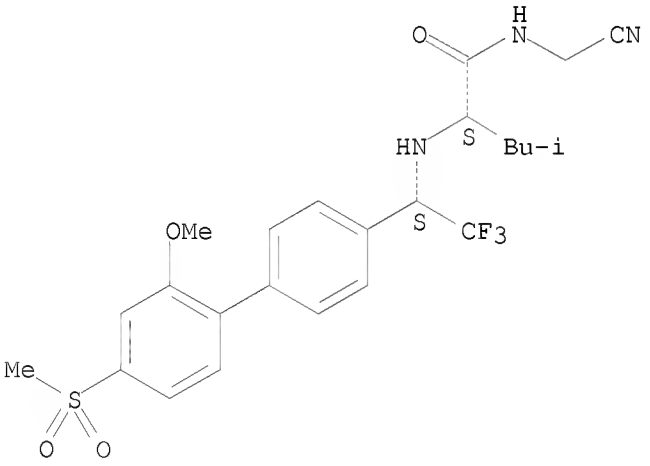
RN 603141-06-6 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4''-chloro-4'-(methylsulfonyl)[1,1':2',1''-terphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



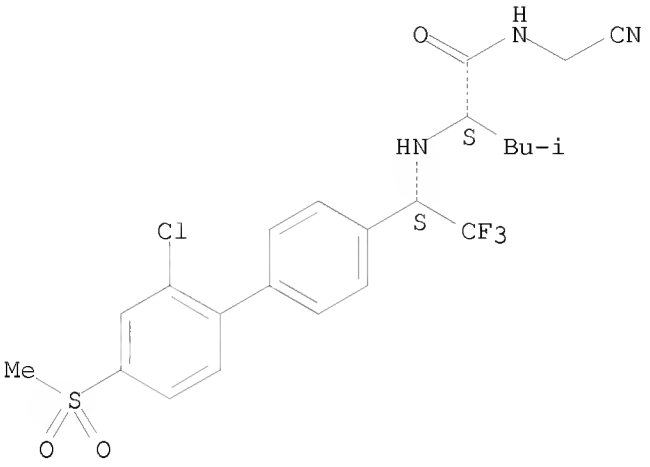
RN 603141-07-7 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[2'-methoxy-4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



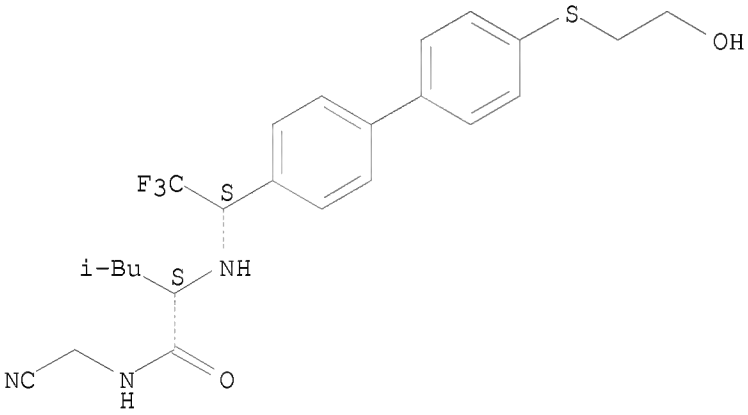
RN 603141-08-8 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[2'-chloro-4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



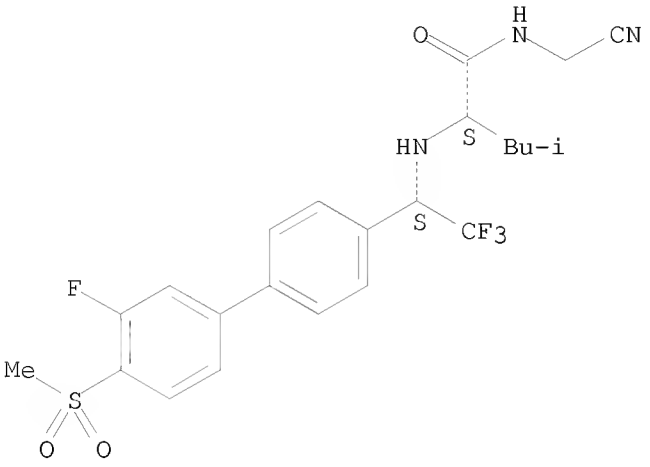
RN 603141-09-9 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-[(2-hydroxyethyl)thio][1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



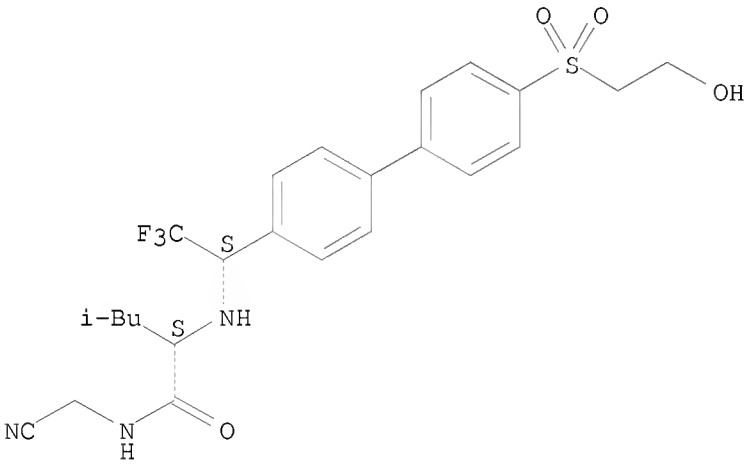
RN 603141-10-2 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[3'-fluoro-4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



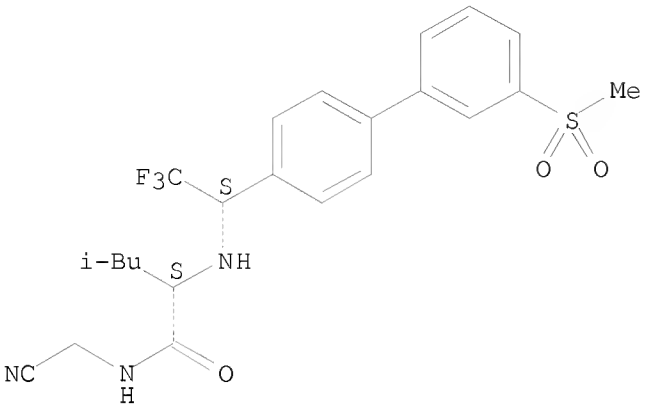
RN 603141-11-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-[(2-hydroxyethyl)sulfonyl][1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



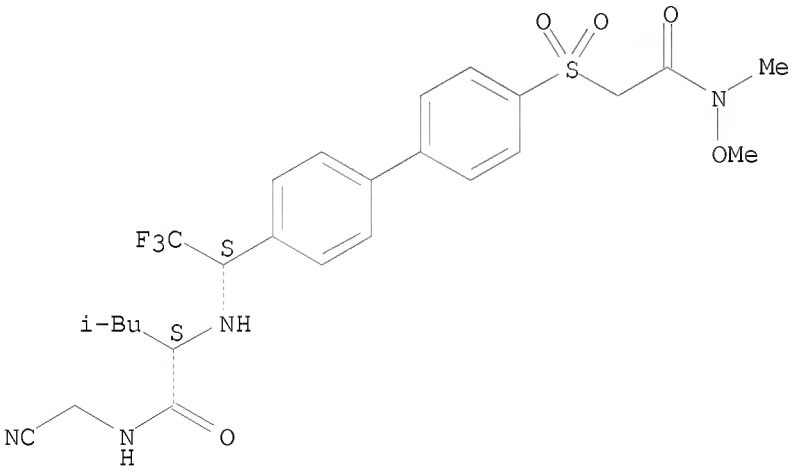
RN 603141-12-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[3'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



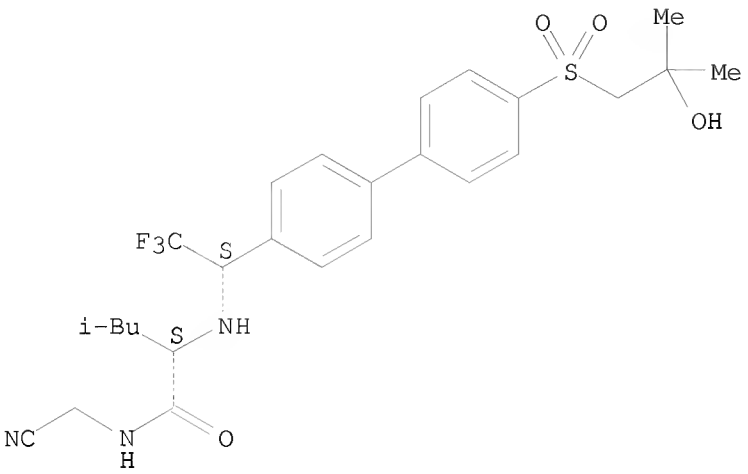
RN 603141-13-5 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-[[2-(methoxymethylamino)-2-oxoethyl]sulfonyl][1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



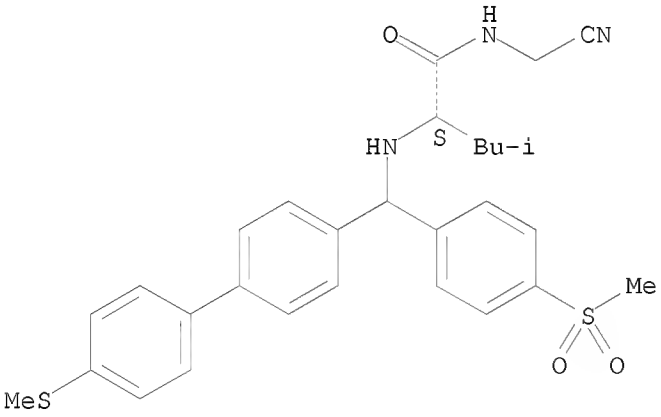
RN 603141-14-6 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-[(2-hydroxy-2-methylpropyl)sulfonyl][1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



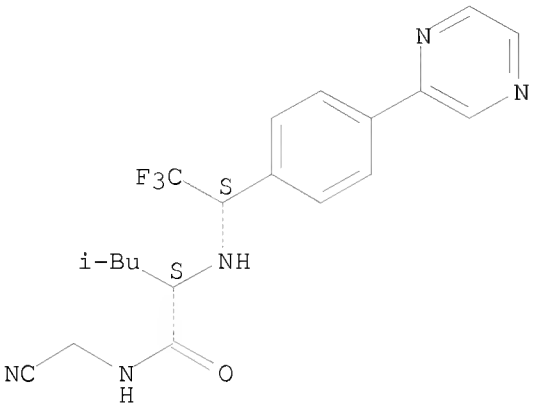
RN 603141-16-8 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[[4-(methylsulfonyl)phenyl][4'-(methylthio)[1,1'-biphenyl]-4-yl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



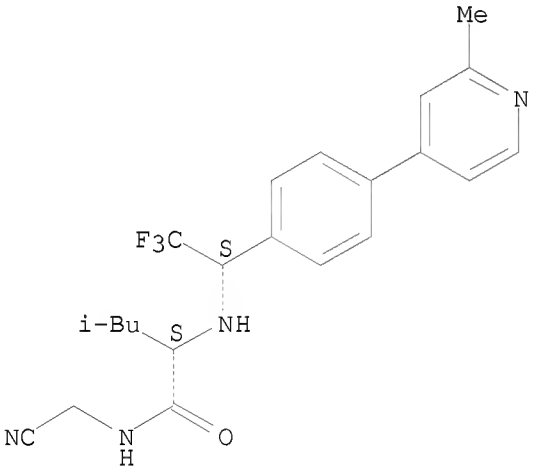
RN 603141-20-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(2-pyrazinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



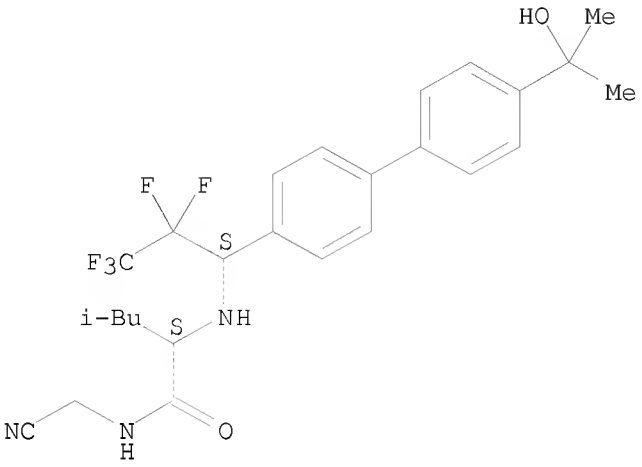
RN 603141-21-5 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(2-methyl-4-pyridinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



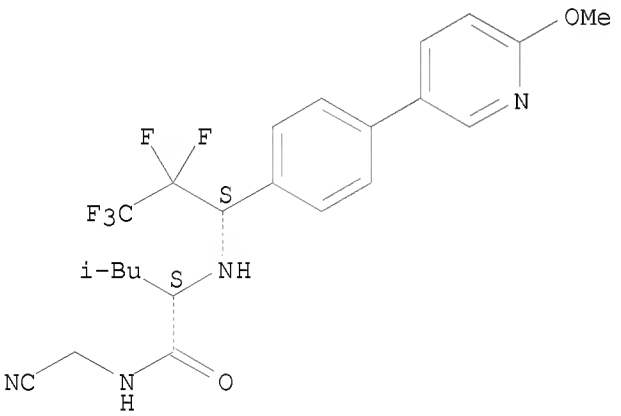
RN 603141-27-1 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,3,3,3-pentafluoro-1-[4'-(1-hydroxy-1-methylethyl)[1,1'-biphenyl]-4-yl]propyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



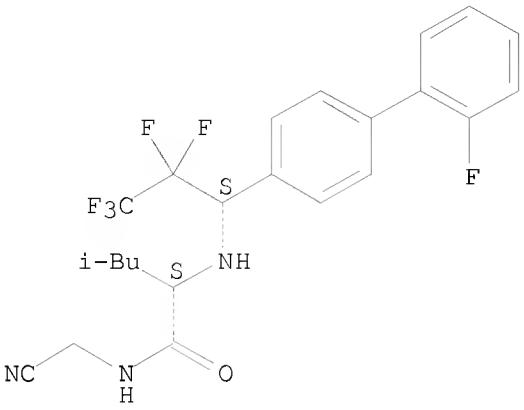
RN 603141-29-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,3,3,3-pentafluoro-1-[4-(6-methoxy-3-pyridinyl)phenyl]propyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



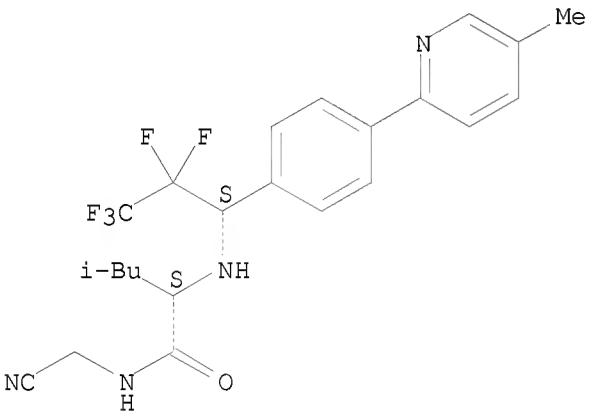
RN 603141-30-6 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,3,3,3-pentafluoro-1-(2'-fluoro[1,1'-biphenyl]-4-yl)propyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



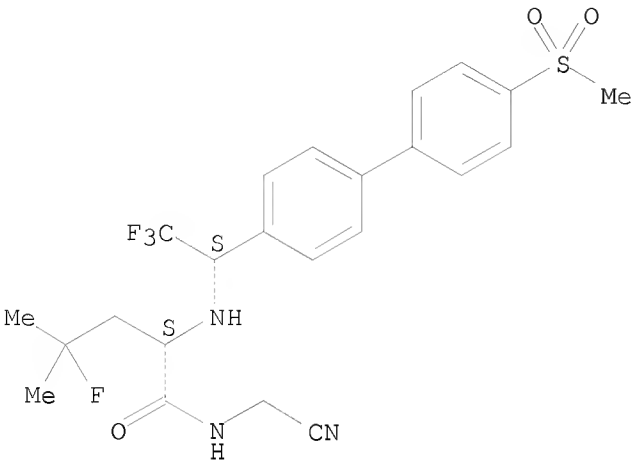
RN 603141-34-0 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,3,3,3-pentafluoro-1-[4-(5-methyl-2-pyridinyl)phenyl]propyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



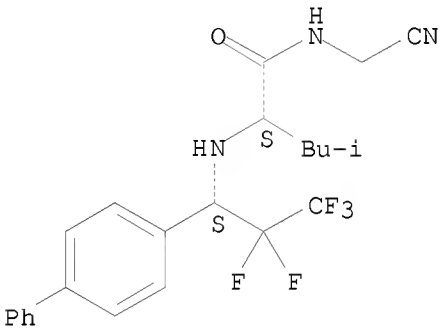
RN 603141-37-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-fluoro-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



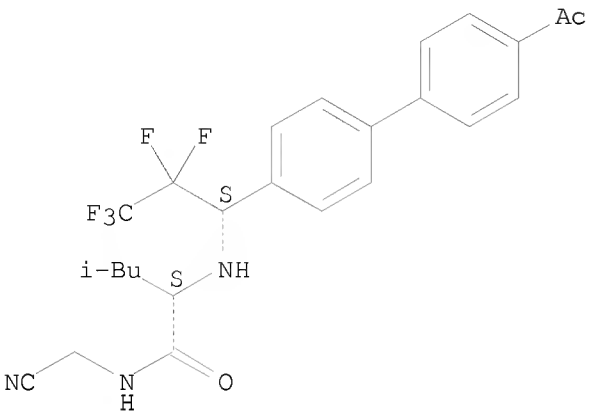
RN 603141-55-5 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[1,1'-biphenyl]-4-yl-2,2,3,3,3-pentafluoropropyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



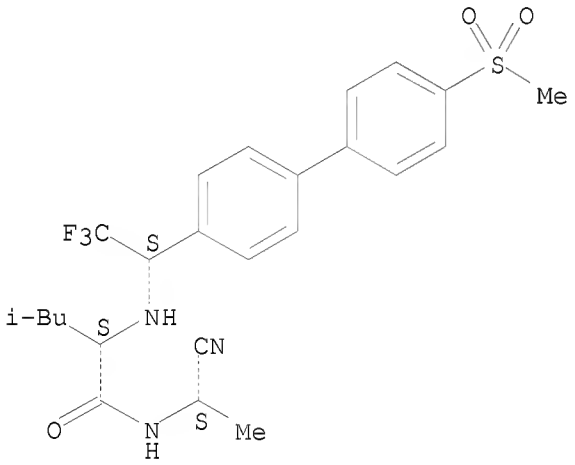
RN 603141-56-6 CAPLUS
CN Pentanamide, 2-[[(1S)-1-(4'-acetyl[1,1'-biphenyl]-4-yl)-2,2,3,3,3-pentafluoropropyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



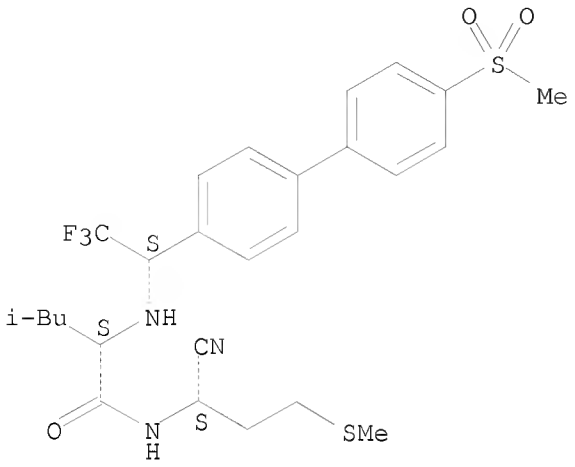
RN 603141-69-1 CAPLUS
CN Pentanamide, N-[(1S)-1-cyanoethyl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



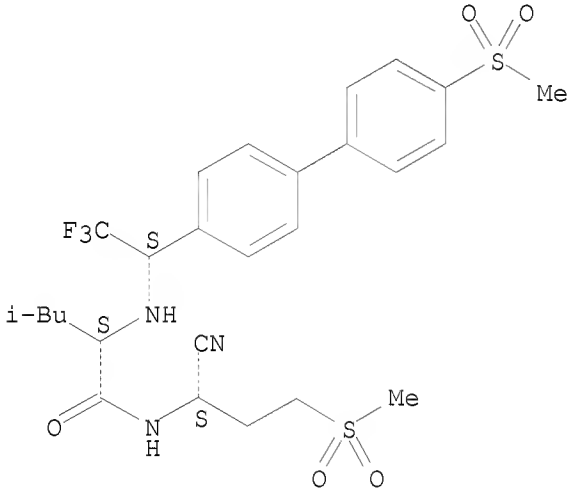
RN 603141-70-4 CAPLUS
CN Pentanamide, N-[(1S)-1-cyano-3-(methylthio)propyl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



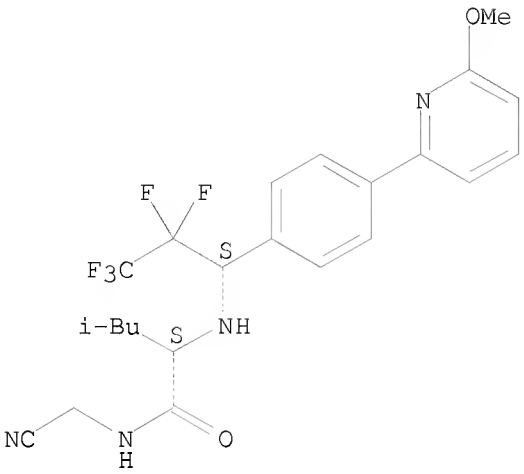
RN 603141-71-5 CAPLUS
CN Pentanamide, N-[(1S)-1-cyano-3-(methylsulfonyl)propyl]-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



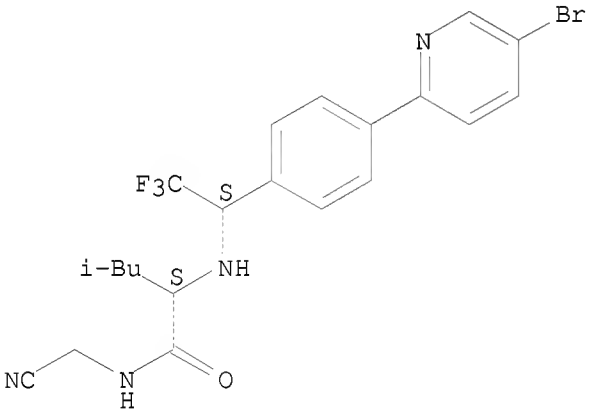
RN 603141-73-7 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,3,3,3-pentafluoro-1-[4-(6-methoxy-2-pyridinyl)phenyl]propyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



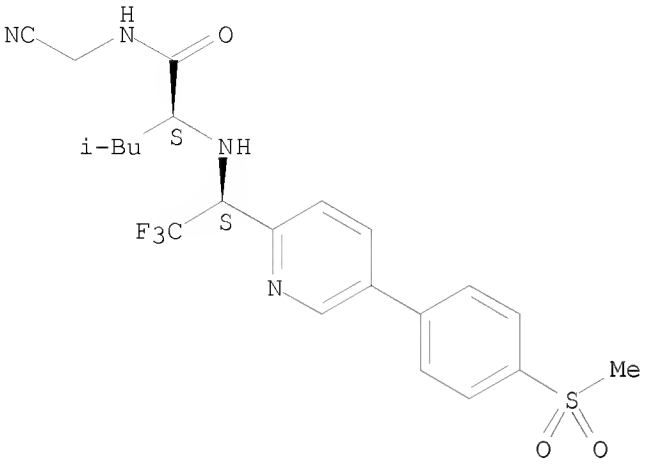
RN 603141-74-8 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4-(5-bromo-2-pyridinyl)phenyl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



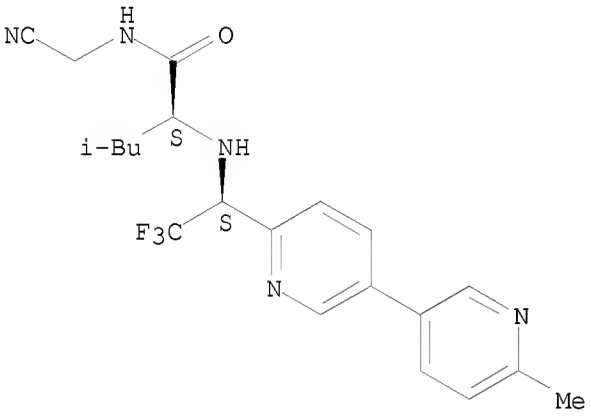
RN 603141-75-9 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[5-[4-(methylsulfonyl)phenyl]-2-pyridinyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



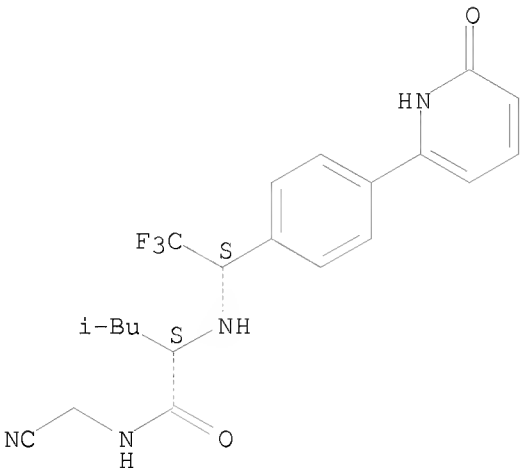
RN 603141-77-1 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-(6'-methyl[3,3'-bipyridin]-6-yl)ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



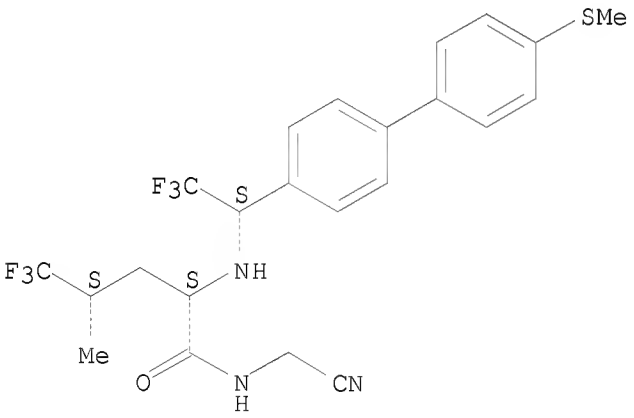
RN 603141-79-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[(1S)-1-[4-(1,6-dihydro-6-oxo-2-pyridinyl)phenyl]-2,2,2-trifluoroethyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



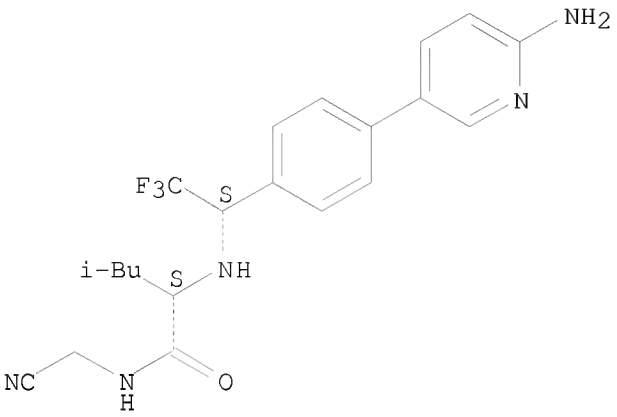
RN 603141-80-6 CAPLUS
CN Pentanamide, N-(cyanomethyl)-5,5,5-trifluoro-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylthio)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S,4S)-(CA INDEX NAME)

Absolute stereochemistry.



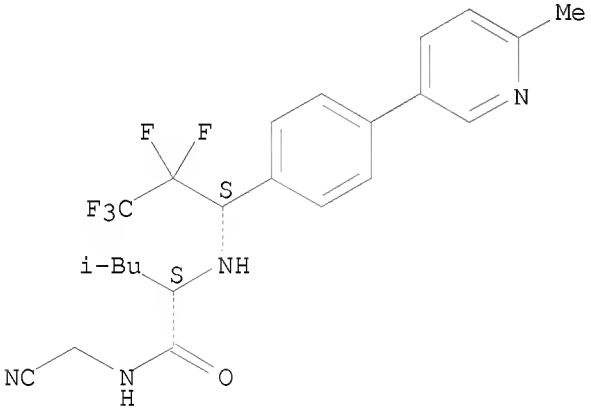
RN 603141-84-0 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4-(6-amino-3-pyridinyl)phenyl]-2,2,2-trifluoroethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



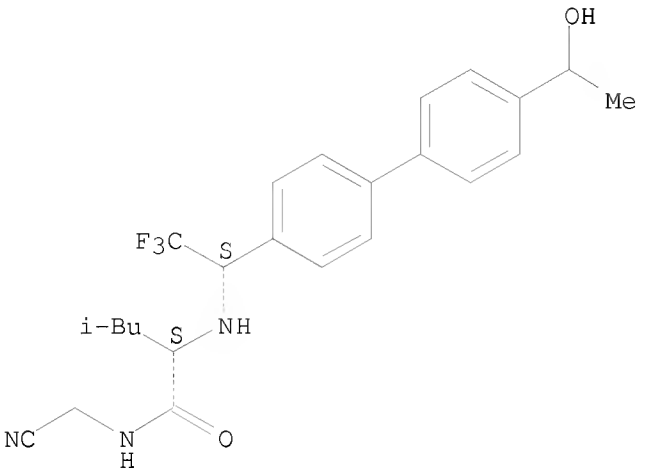
RN 603141-86-2 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,3,3,3-pentafluoro-1-[4-(6-methyl-3-pyridinyl)phenyl]propyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



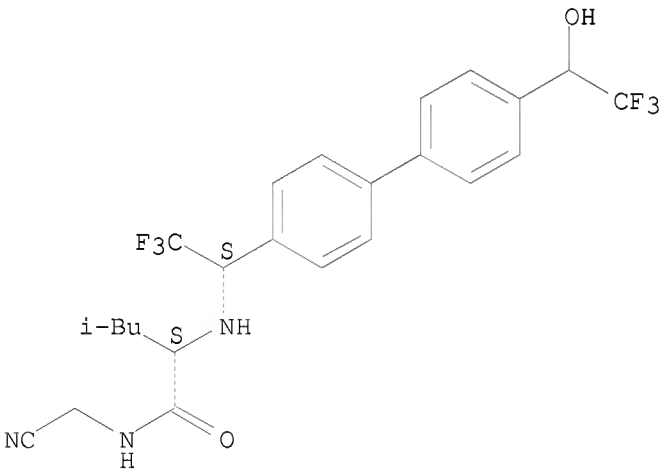
RN 603141-89-5 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(1-hydroxyethyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



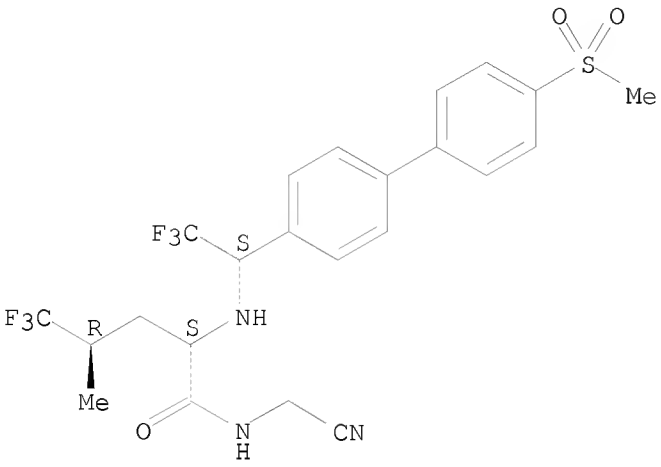
RN 603141-90-8 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(2,2,2-trifluoro-1-hydroxyethyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



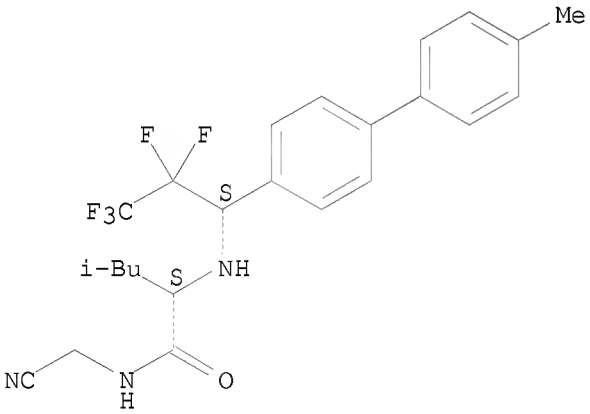
RN 603141-93-1 CAPLUS
CN Pentanamide, N-(cyanomethyl)-5,5,5-trifluoro-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S,4R)- (CA INDEX NAME)

Absolute stereochemistry.



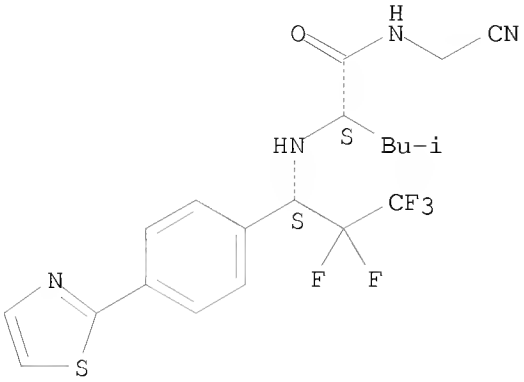
RN 603141-95-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,3,3,3-pentafluoro-1-(4'-methyl[1,1'-biphenyl]-4-yl)propyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



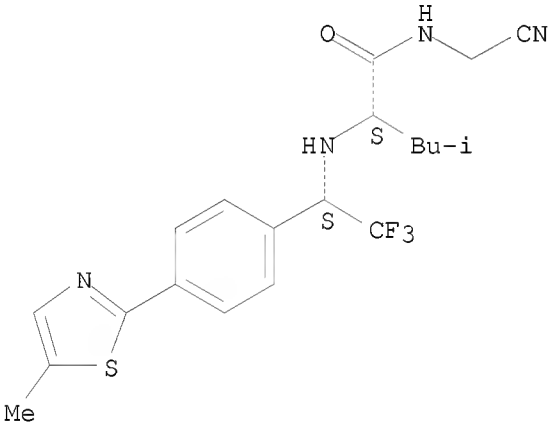
RN 603141-96-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,3,3,3-pentafluoro-1-[4-(2-thiazolyl)phenyl]propyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



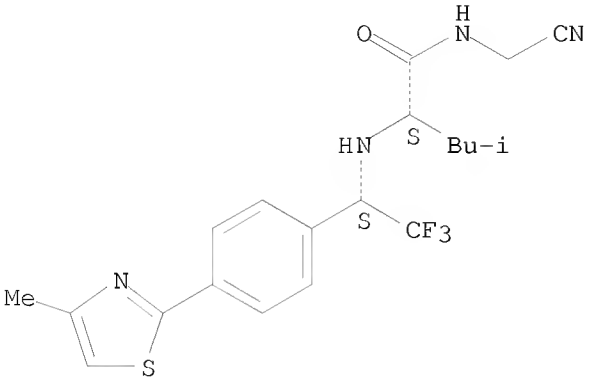
RN 603142-00-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(5-methyl-2-thiazolyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



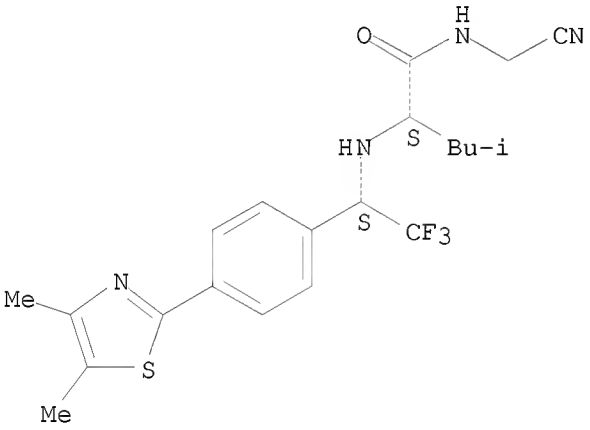
RN 603142-05-8 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(4-methyl-2-thiazolyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



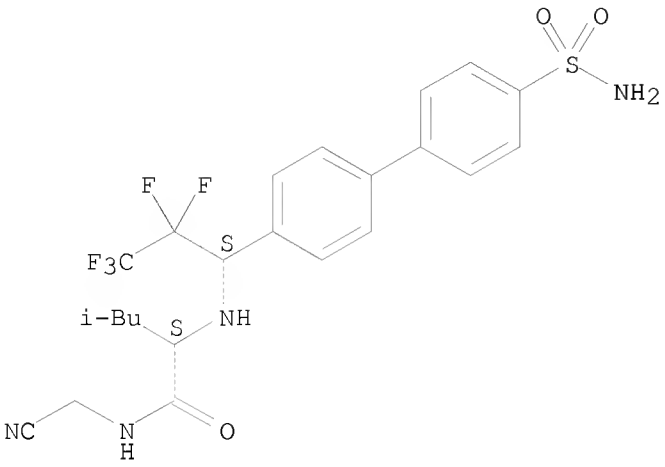
RN 603142-06-9 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[(1S)-1-[4-(4,5-dimethyl-2-thiazolyl)phenyl]-2,2,2-trifluoroethyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



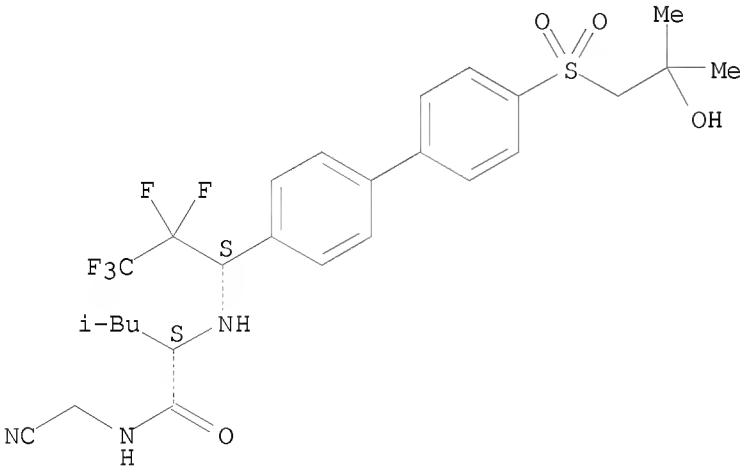
RN 603142-11-6 CAPLUS
CN Pentanamide, 2-[[(1S)-1-[4'-(aminosulfonyl)[1,1'-biphenyl]-4-yl]-2,2,3,3,3-pentafluoropropyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



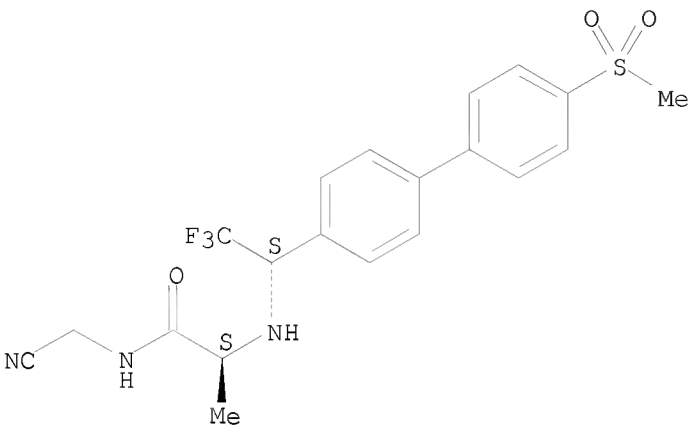
RN 603142-12-7 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,3,3,3-pentafluoro-1-[4'-[(2-hydroxy-2-methylpropyl)sulfonyl][1,1'-biphenyl]-4-yl]propyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



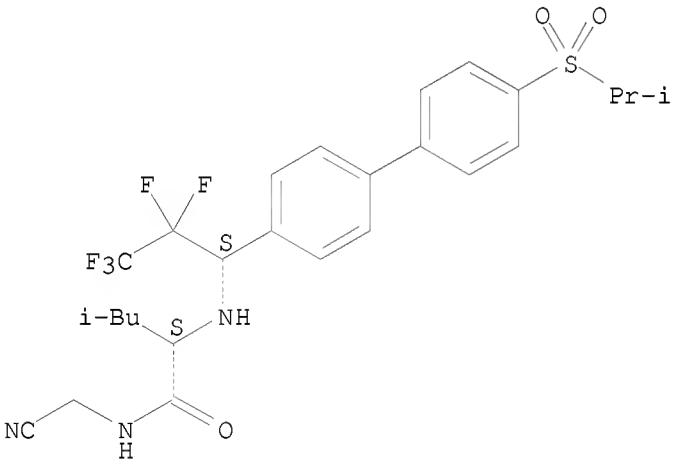
RN 603142-13-8 CAPLUS
CN Propanamide, N-(cyanomethyl)-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



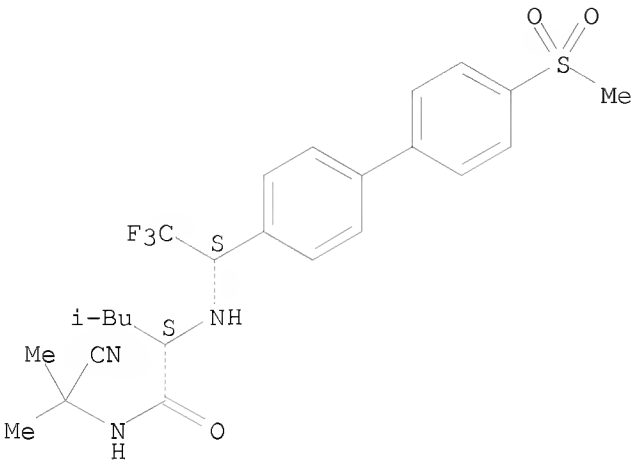
RN 603142-14-9 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,3,3,3-pentafluoro-1-[4'-[(1-methylethyl)sulfonyl][1,1'-biphenyl]-4-yl]propyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



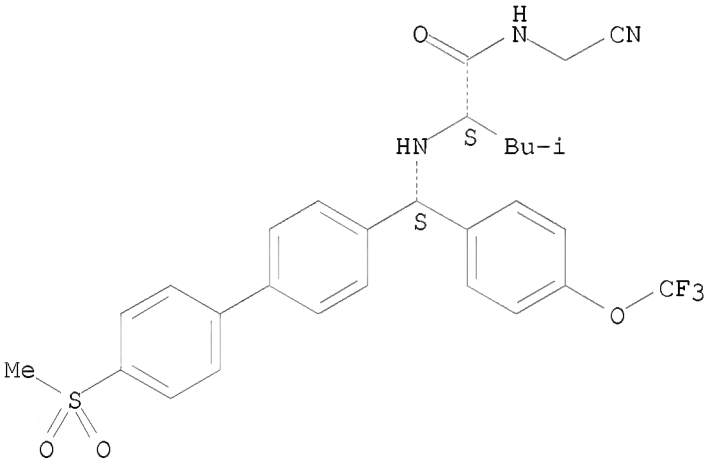
RN 603142-15-0 CAPLUS
CN Pentanamide, N-(1-cyano-1-methylethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



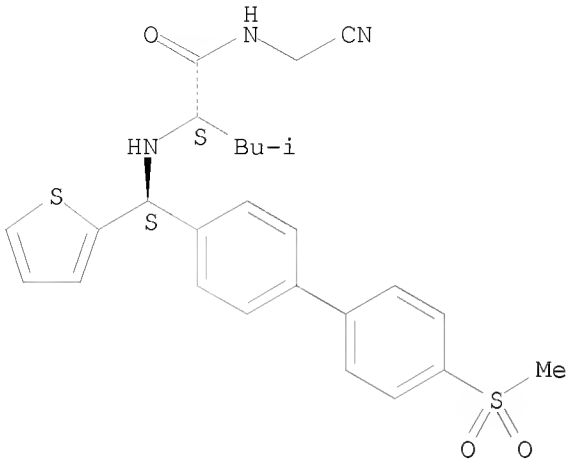
RN 603142-20-7 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(S)-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl][4-(trifluoromethoxy)phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



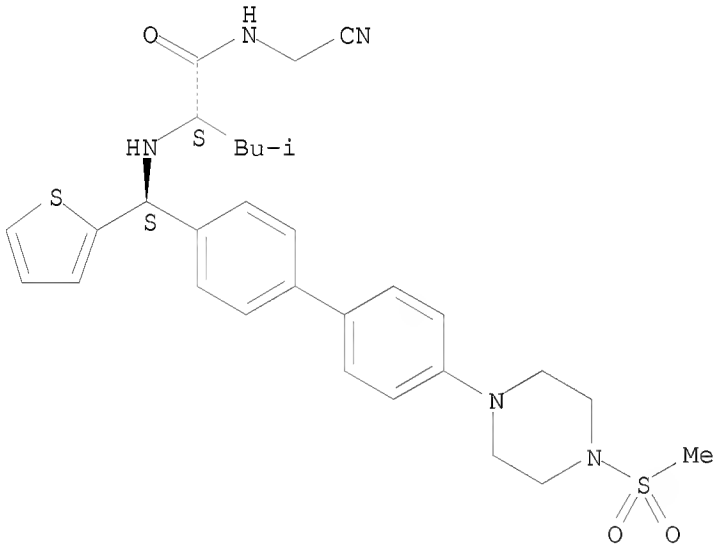
RN 603142-21-8 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(S)-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]-2-thienylmethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



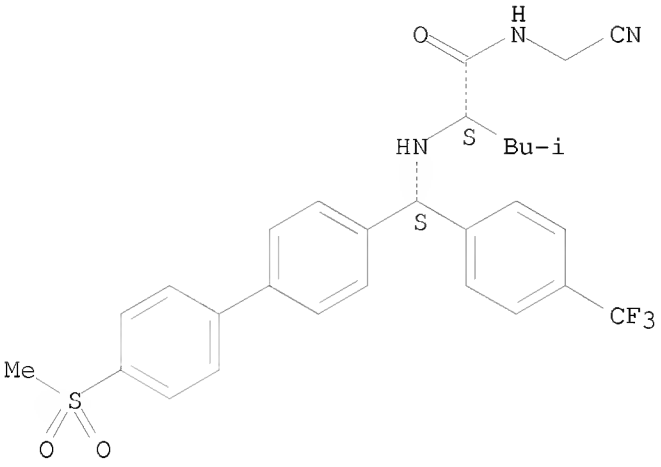
RN 603142-22-9 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(S)-[4'-[4-(methylsulfonyl)-1-piperazinyl][1,1'-biphenyl]-4-yl]-2-thienylmethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



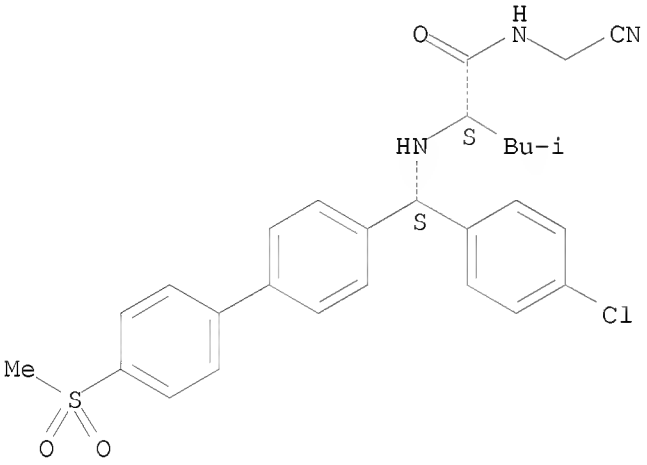
RN 603142-23-0 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(S)-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl][4-(trifluoromethyl)phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



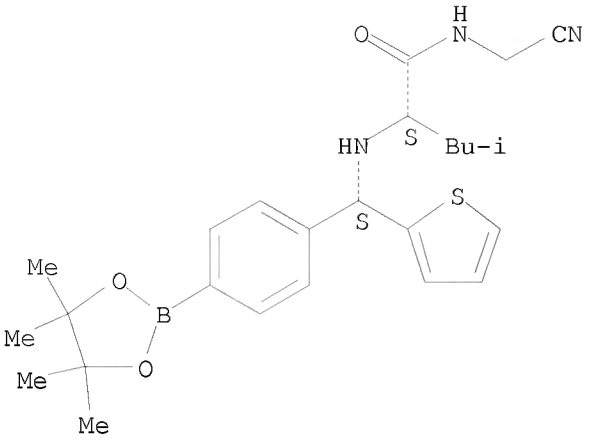
RN 603142-24-1 CAPLUS
CN Pentanamide, 2-[[(S)-(4-chlorophenyl)[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]methyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



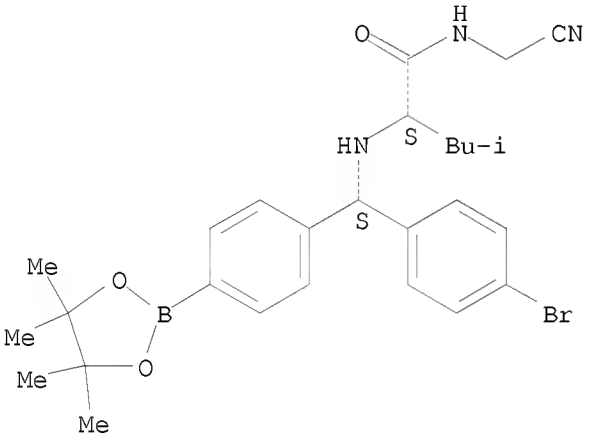
RN 603142-26-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(S)-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]-2-thienylmethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



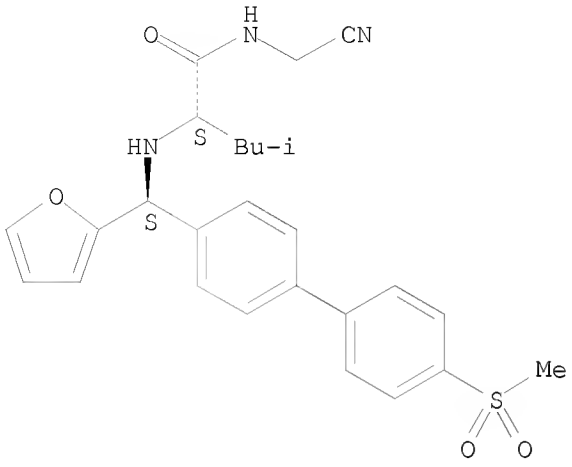
RN 603142-28-5 CAPLUS
CN Pentanamide, 2-[[(S)-(4-bromophenyl)[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]methyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



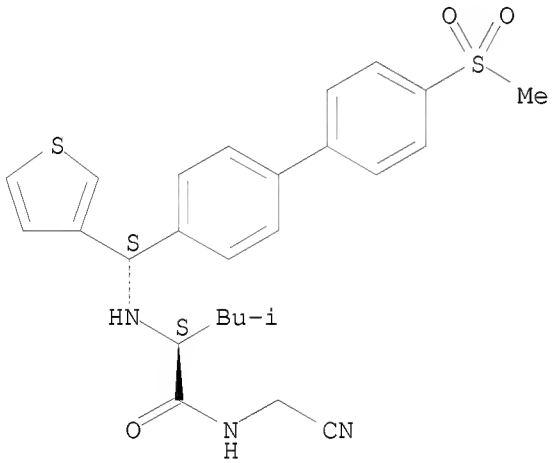
RN 603142-30-9 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[(S)-2-furanyl[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]methyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



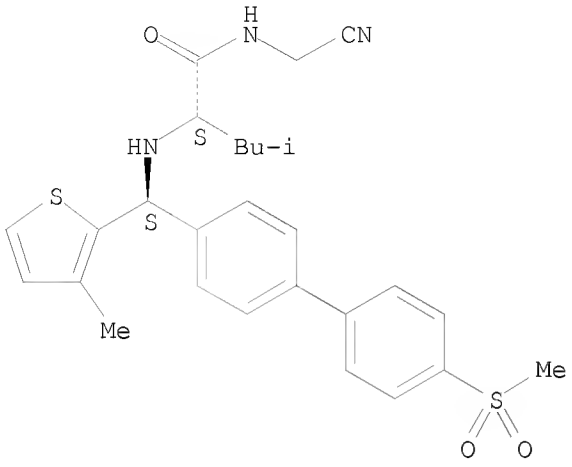
RN 603142-35-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(S)-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]-3-thienylmethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



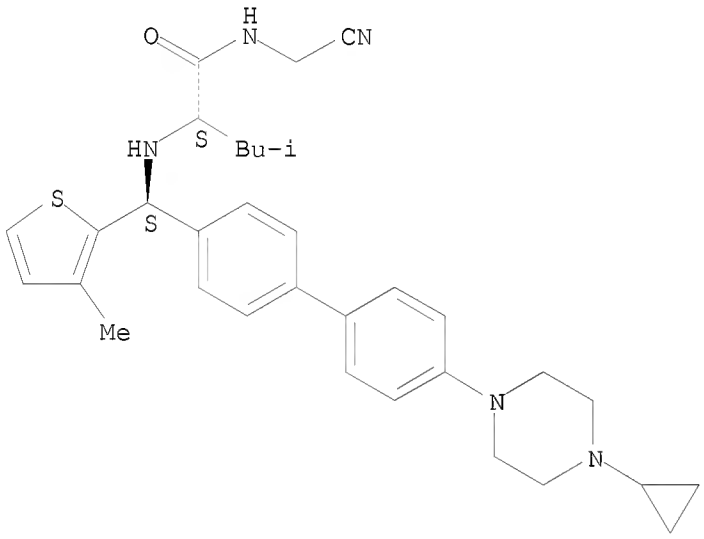
RN 603142-36-5 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(S)-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl](3-methyl-2-thienyl)methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



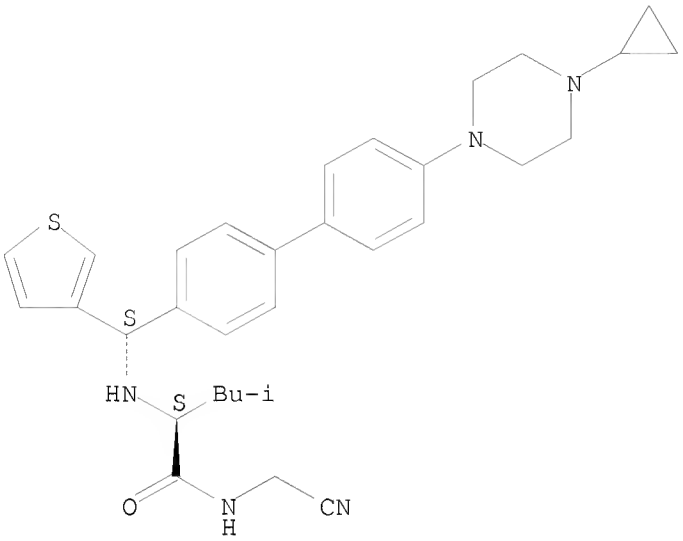
RN 603142-37-6 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[(S)-[4'-(4-cyclopropyl-1-piperazinyl)[1,1'-biphenyl]-4-yl](3-methyl-2-thienyl)methyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



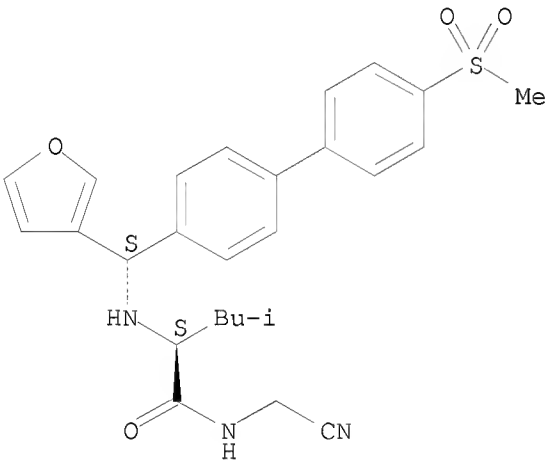
RN 603142-38-7 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[(S)-[4'-(4-cyclopropyl-1-piperazinyl)[1,1'-biphenyl]-4-yl]-3-thienylmethyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



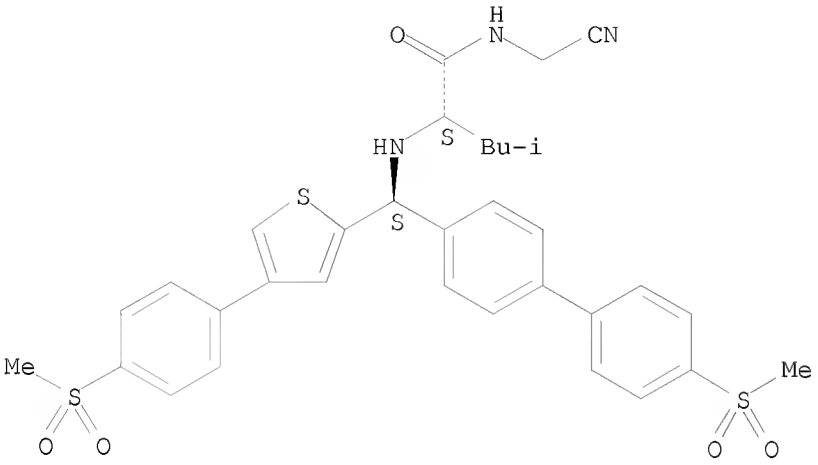
RN 603142-42-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[(S)-3-furanyl[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]methyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



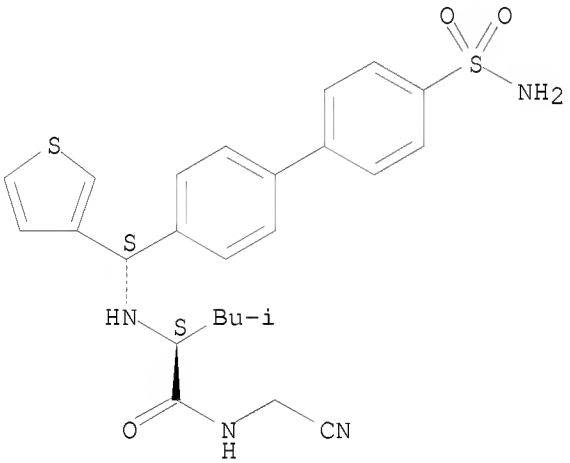
RN 603142-45-6 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(S)-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl][4-[4-(methylsulfonyl)phenyl]-2-thienyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



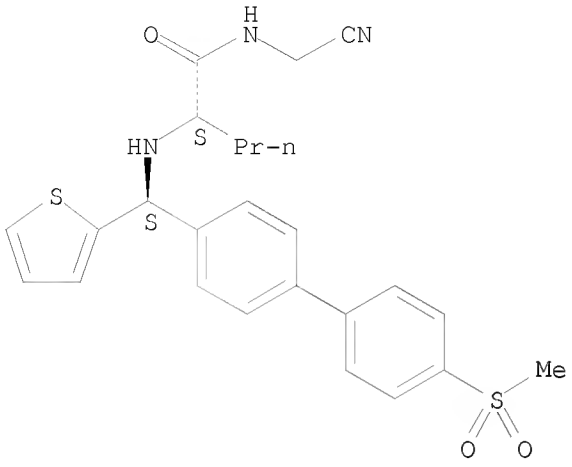
RN 603142-49-0 CAPLUS
CN Pentanamide, 2-[[(S)-[4'-(aminosulfonyl)[1,1'-biphenyl]-4-yl]-3-thienylmethyl]amino]-N-(cyanomethyl)-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



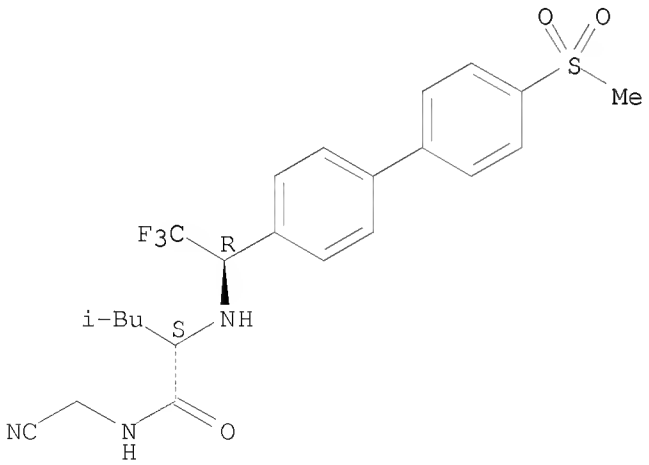
RN 603142-70-7 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[(S)-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]-2-thienylmethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



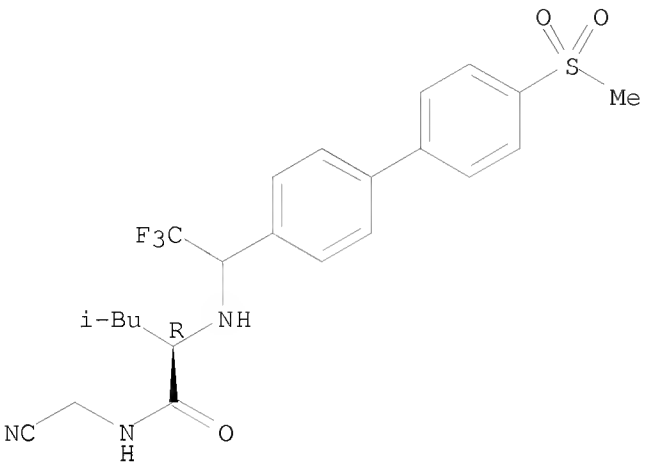
IT 603143-34-6 603143-36-8 603143-37-9
603143-38-0 603143-40-4 603143-46-0
603143-48-2 603143-50-6 603143-51-7
603143-63-1 603143-64-2 603143-67-5
603143-92-6 603143-94-8 603143-96-0
603143-98-2 603144-00-9 603144-78-1
603144-79-2 603145-26-2 603145-48-8
603145-51-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cathepsin cysteine protease inhibitors and their therapeutic use)
RN 603143-34-6 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1R)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



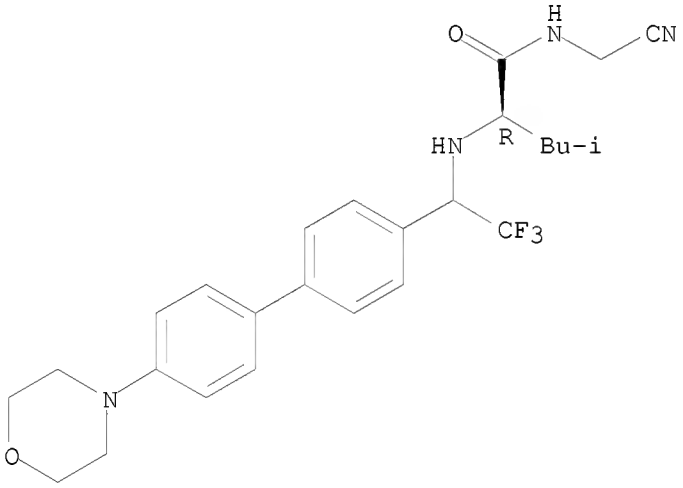
RN 603143-36-8 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.



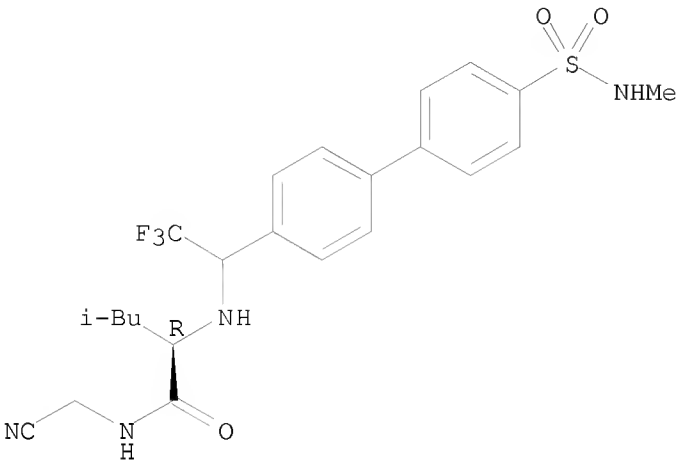
RN 603143-37-9 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4'-(4-morpholinyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.



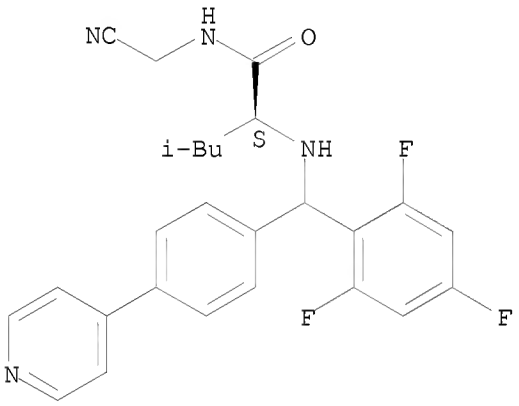
RN 603143-38-0 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[2,2,2-trifluoro-1-[4'-[(methylamino)sulfonyl][1,1'-biphenyl]-4-yl]ethyl]amino]-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.



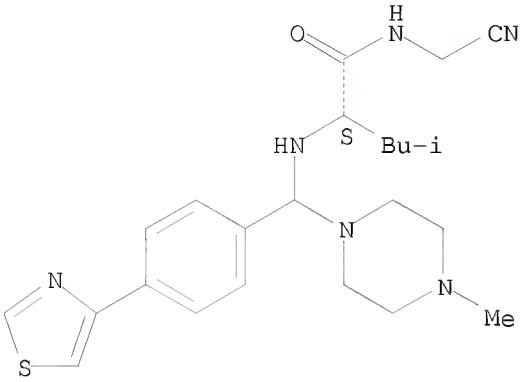
RN 603143-40-4 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[[4-(4-pyridinyl)phenyl](2,4,6-trifluorophenyl)methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



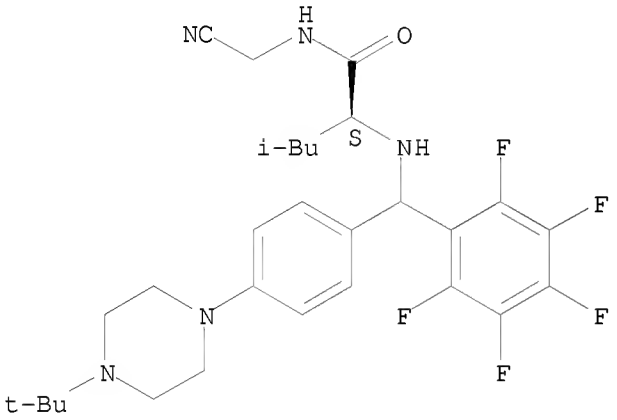
RN 603143-46-0 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(4-methyl-1-piperazinyl)[4-(4-thiazolyl)phenyl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



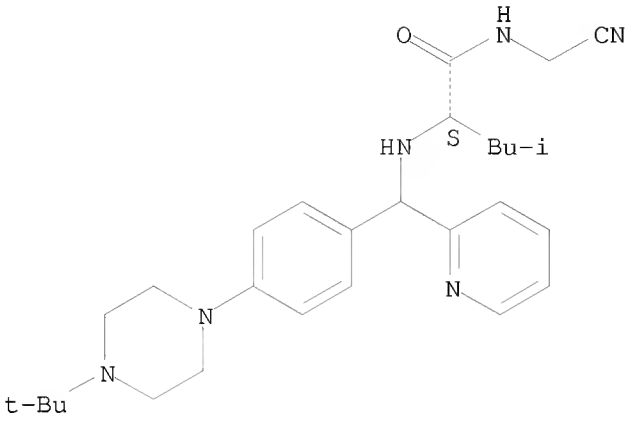
RN 603143-48-2 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[[4-[4-(1,1-dimethylethyl)-1-piperazinyl]phenyl](2,3,4,5,6-pentafluorophenyl)methyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



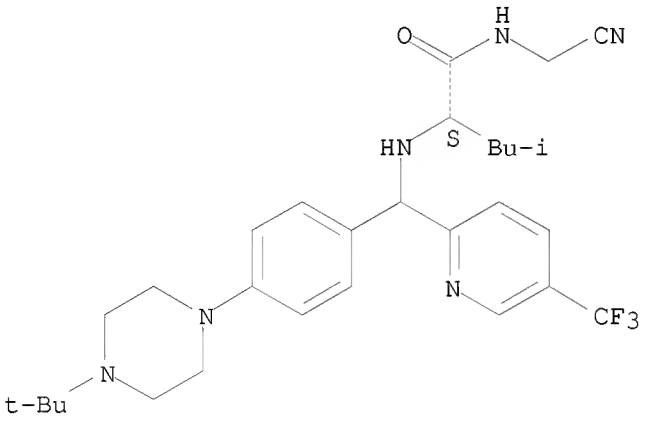
RN 603143-50-6 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[[4-[4-(1,1-dimethylethyl)-1-piperazinyl]phenyl]-2-pyridinylmethyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



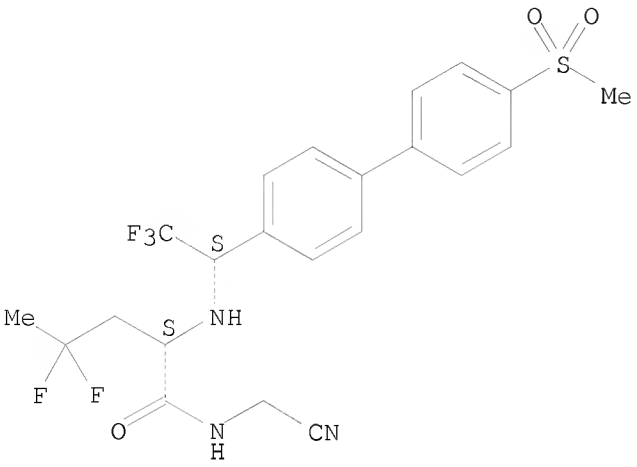
RN 603143-51-7 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[[4-[4-(1,1-dimethylethyl)-1-piperazinyl]phenyl][5-(trifluoromethyl)-2-pyridinyl]methyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



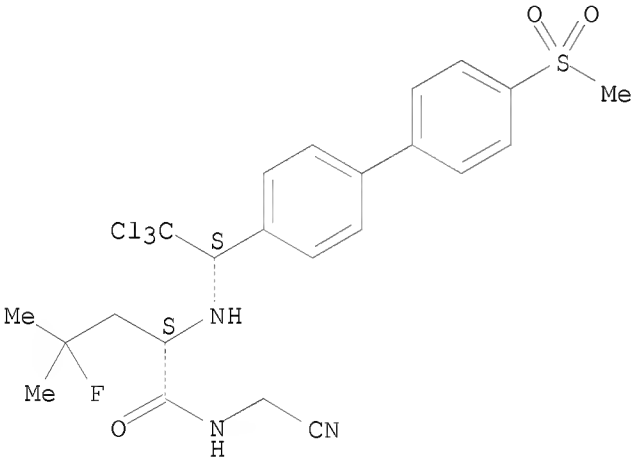
RN 603143-63-1 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4,4-difluoro-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



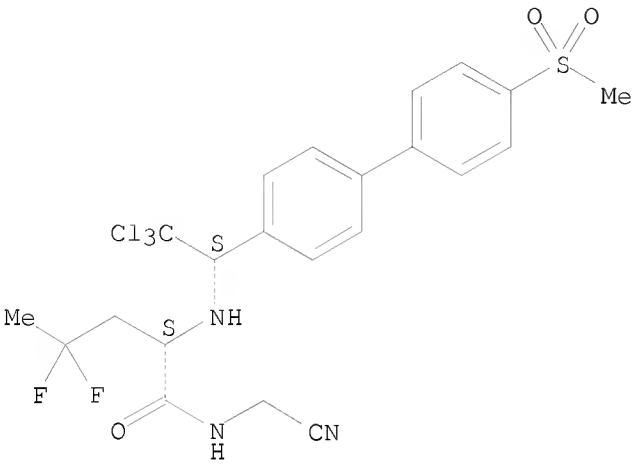
RN 603143-64-2 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-fluoro-4-methyl-2-[[(1S)-2,2,2-trichloro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



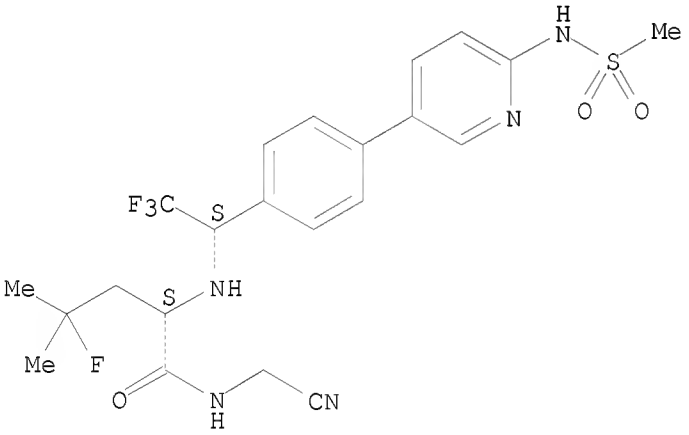
RN 603143-67-5 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4,4-difluoro-2-[[(1S)-2,2,2-trichloro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



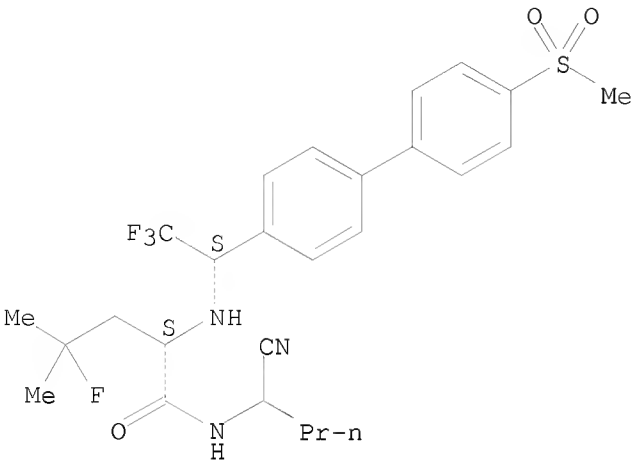
RN 603143-92-6 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-fluoro-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-[6-[(methylsulfonyl)amino]-3-pyridinyl]phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



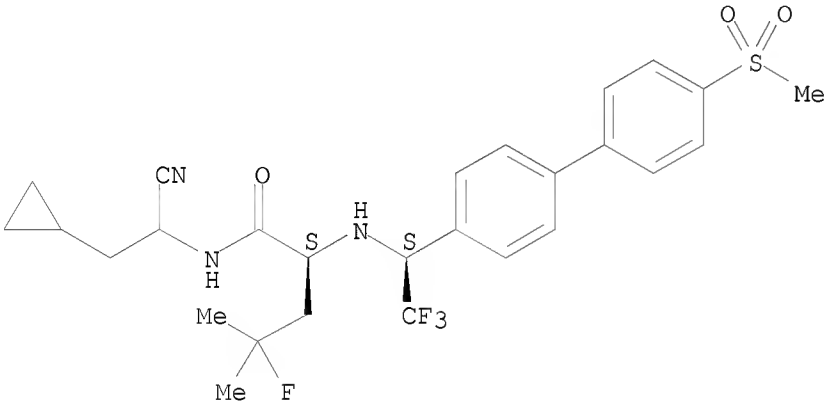
RN 603143-94-8 CAPLUS
CN Pentanamide, N-(1-cyanobutyl)-4-fluoro-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



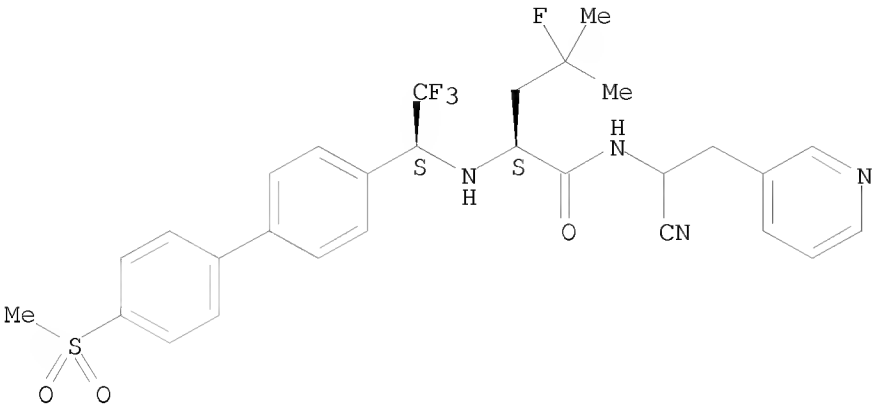
RN 603143-96-0 CAPLUS
CN Pentanamide, N-(1-cyano-2-cyclopropylethyl)-4-fluoro-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



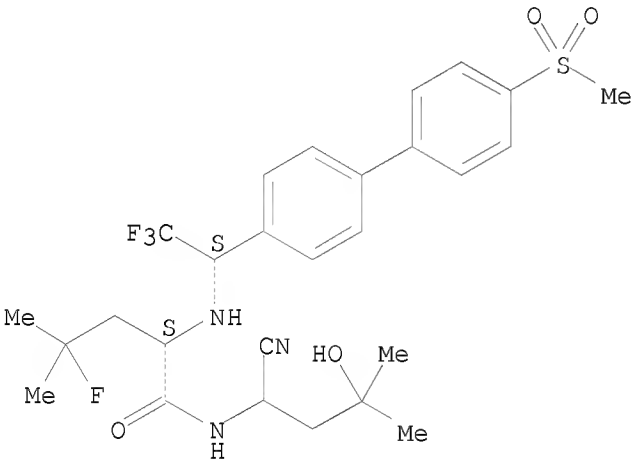
RN 603143-98-2 CAPLUS
CN Pentanamide, N-[1-cyano-2-(3-pyridinyl)ethyl]-4-fluoro-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



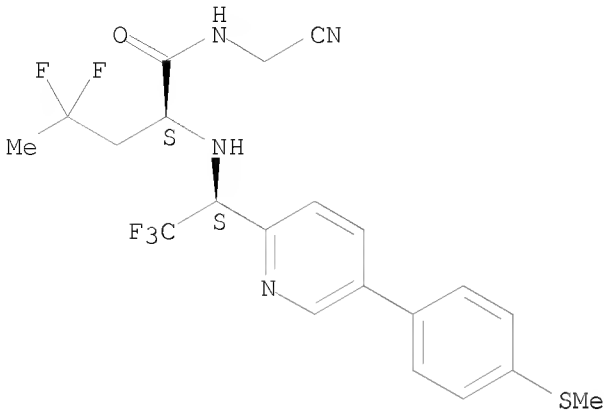
RN 603144-00-9 CAPLUS
CN Pentanamide, N-(1-cyano-3-hydroxy-3-methylbutyl)-4-fluoro-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



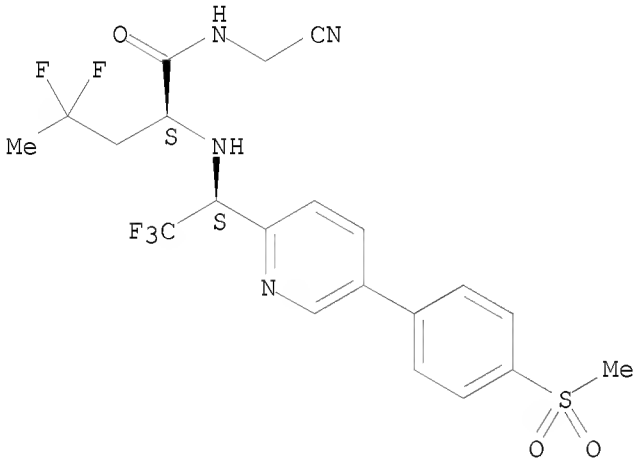
RN 603144-78-1 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4,4-difluoro-2-[[(1S)-2,2,2-trifluoro-1-[5-[4-(methylthio)phenyl]-2-pyridinyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



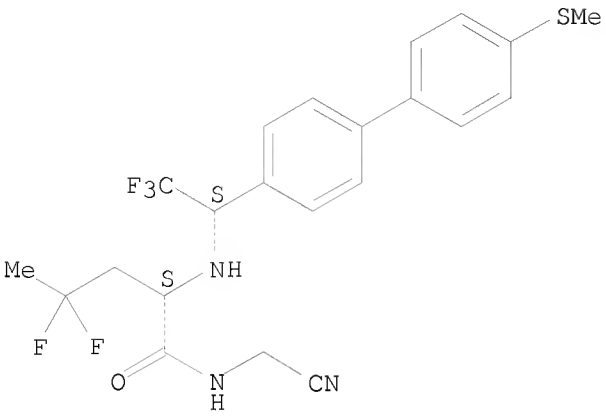
RN 603144-79-2 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4,4-difluoro-2-[[(1S)-2,2,2-trifluoro-1-[5-[4-(methylsulfonyl)phenyl]-2-pyridinyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



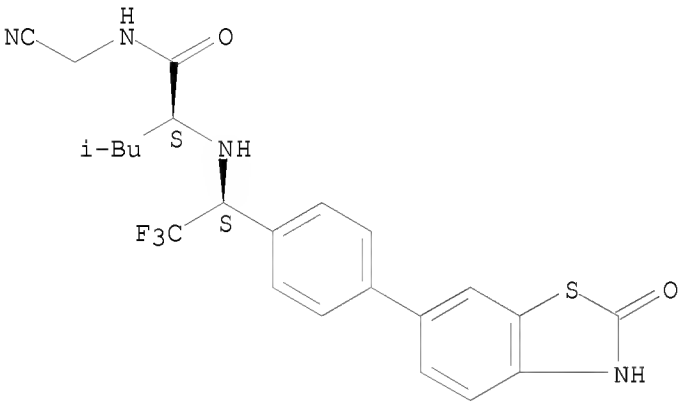
RN 603145-26-2 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4,4-difluoro-2-[[(1S)-2,2,2-trifluoro-1-[4'-(methylthio)[1,1'-biphenyl]-4-yl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



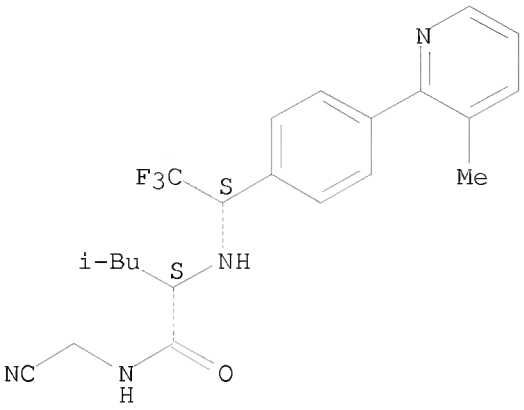
RN 603145-48-8 CAPLUS
CN Pentanamide, N-(cyanomethyl)-2-[[(1S)-1-[4-(2,3-dihydro-2-oxo-6-benzothiazolyl)phenyl]-2,2,2-trifluoroethyl]amino]-4-methyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 603145-51-3 CAPLUS
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[(1S)-2,2,2-trifluoro-1-[4-(3-methyl-2-pyridinyl)phenyl]ethyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 32 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:695723 CAPLUS
DOCUMENT NUMBER: 137:232908
TITLE: Preparation of N-cyanomethyl amides as cathepsin cysteine protease inhibitors
INVENTOR(S): Prasit, Petpiboon; Bayly, Christopher Ian; Robichaud, Joel Stephane; Black, W. Cameron; Setti, Eduardo L.; Rydzewski, Robert M.; Palmer, James T.
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.; PE Corporation (NY); AXYS Pharm. Inc.
SOURCE: PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002069901	A2	20020912	WO 2002-US6533	20020301
WO 2002069901	A3	20031030		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2439415	A1	20020912	CA 2002-2439415	20020301
AU 2002254099	A1	20020919	AU 2002-254099	20020301
AU 2002254099	B2	20060706		
EP 1372655	A2	20040102	EP 2002-723314	20020301
EP 1372655	B1	20081001		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004531486	T	20041014	JP 2002-569079	20020301

AT 409482	T	20081015	AT 2002-723314		20020301
US 20040198982	A1	20041007	US 2003-469430		20030828
US 7012075	B2	20060314			
PRIORITY APPLN. INFO.:			US 2001-272799P	P	20010302
			WO 2002-US6533	W	20020301

OTHER SOURCE(S): MARPAT 137:232908

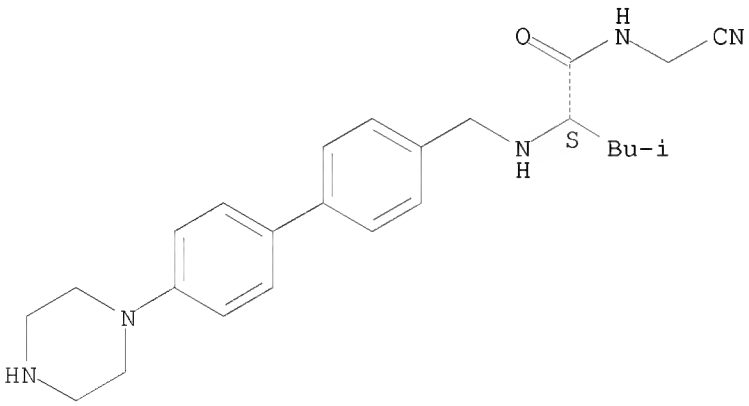
AB The invention relates to a novel class of compds. R5-(E)n-D-X-CR3R4CONHCR1R2CN [R1 = H, (halo)alkyl, or (halo)alkenyl or R1R2C is a cycloalkyl ring optionally substituted by alkyl, hydroxyalkyl, or halogen; R3, R4 = H, alkyl or alkenyl optionally substituted by cycloalkyl or halogen or R3R4C is cycloalkyl, cycloalkenyl or heterocyclyl optionally substituted by alkyl, halo, hydroxyalkyl, hydroxy, alkoxy, or keto; X = NH, NR6, NHSO2, O, CR7R8O, OCR7R8, CR7R8CR7R8O, S, SO2, CR7R8S, SCR7R8, CR7R8SO2, SO2CR7R8, CR7R8, CR7R8NR7, NR7CR7R8, where R6 = alkyl or R6 and R4 form a 4-12 membered heterocyclyl ring system which is optionally substituted and R7, R8 = H or alkyl; D, E = (un)substituted aryl, heteroaryl, cycloalkyl, or heterocyclyl; n = 1-2; R5 = H, alkyl, alkenyl, alkoxy, halo, nitro, cyano, amino, aryl, heteroaryl, cycloalkyl, heterocyclyl, CO2H, OH, alkoxy, SH, sulfonyl groups, etc.] and their pharmaceutically-acceptable salts and N-oxide derivs. are cysteine protease inhibitors and are useful for treating diseases in which inhibition of bone resorption is indicated, such as osteoporosis. Thus, C4H9N2-p-C6H4-p-C6H4-L-Leu-NHCH2CN (C4H9N2 = 1-piperazinyl) was prepared from L-leucine, 1,4-dibromobenzene, aminoacetonitrile hydrochloride, and 4-[4-(tert-butoxycarbonyl)-1-piperazinyl]phenylboronic acid (preparation given). The product was used to prepare a pharmaceutical composition

IT 459160-48-6P 459162-76-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-cyanomethyl amides as cathepsin cysteine protease inhibitors)

RN 459160-48-6 CAPLUS

CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[[4'-(1-piperazinyl)[1,1'-biphenyl]-4-yl]methyl]amino]-, (2S)- (CA INDEX NAME)

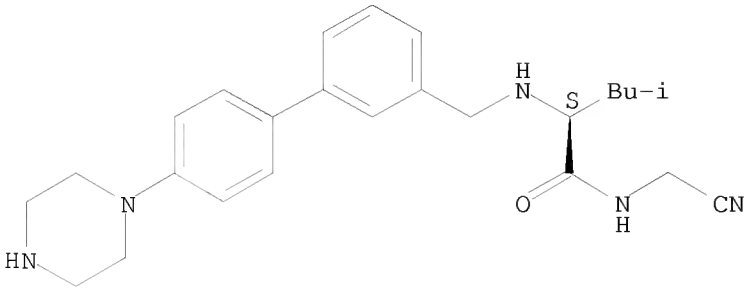
Absolute stereochemistry.



RN 459162-76-6 CAPLUS

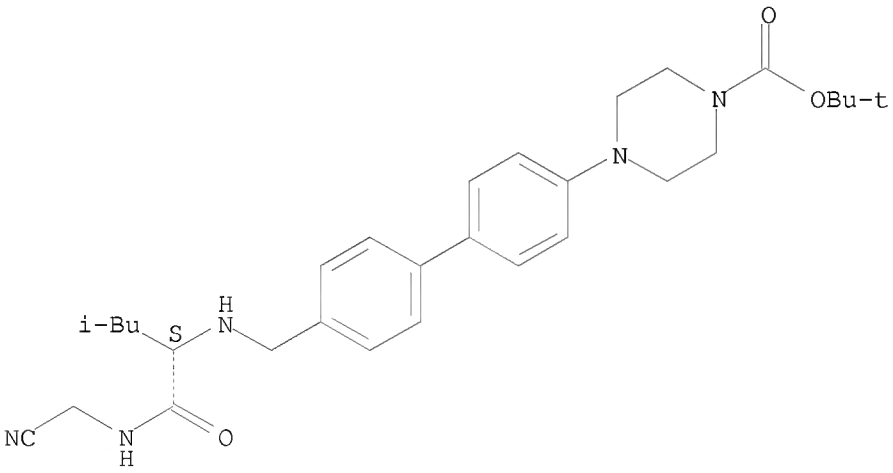
CN Pentanamide, N-(cyanomethyl)-4-methyl-2-[[[4'-(1-piperazinyl)[1,1'-biphenyl]-3-yl]methyl]amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 459164-61-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of N-cyanomethyl amides as cathepsin cysteine protease inhibitors)
RN 459164-61-5 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4'-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]methyl][1,1'-biphenyl]-4-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 33 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:693319 CAPLUS
DOCUMENT NUMBER: 135:257468
TITLE: Preparation of N-(4-thiazolylbenzoyl)-N-(cyanomethyl)-L-leucinamides and analogs as protease inhibitors
INVENTOR(S): Palmer, James T.; Setti, Eduardo L.; Tian, Zong-Qiang; Venkatraman, Shankar; Wang, Dan-Xiong
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 73 pp.

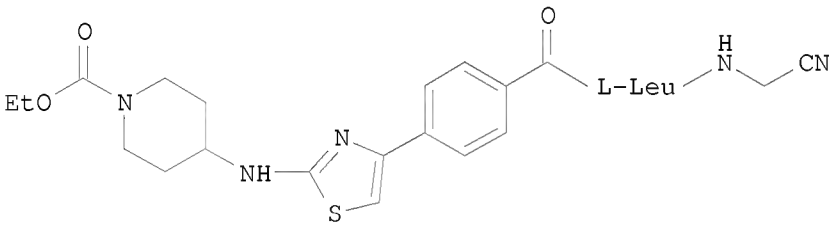
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068645	A2	20010920	WO 2001-US8332	20010314
WO 2001068645	A3	20020307		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-189694P P 20000315
GI



I

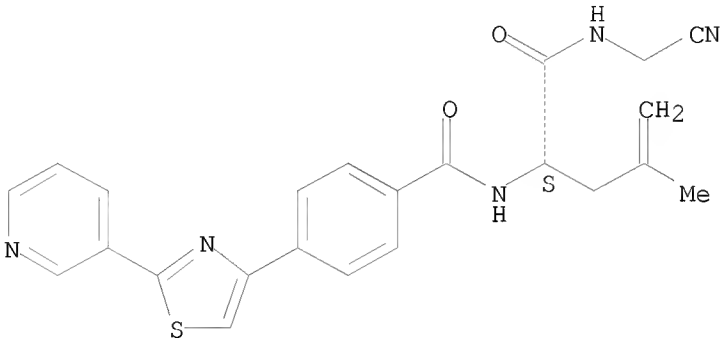
AB The title compds. and their pharmaceutically acceptable salts, N-oxides, prodrugs, protected derivs., or isomers thereof were prepared as cysteine protease inhibitors. For example, stirring a solution of 4-[2-(1-tert-butoxycarbonylpiperidin-4-ylamino)thiazol-4-yl]benzoic acid (preparation given) and the MeSO3H salt of 2S-amino-N-cyanomethyl-4-methylpentanamide overnight at room temperature with PyBOP and diisopropylethylamine in DMF, followed by conversion to the Et ester, yielded I (77%). Test compds. inhibited cathepsin B, K, L, and S (no data). The invention compds. and compns. with a bisphosphonic acid and/or an estrogen receptor agonist are claimed for treating osteoporosis in post-menopausal women (no data).

IT 294622-67-6P 294622-73-4P 294622-74-5P
294622-75-6P 294622-76-7P 294622-77-8P
294622-79-0P 294622-82-5P 294622-83-6P
294622-84-7P 294622-85-8P 294622-86-9P
294622-89-2P 294622-95-0P 294622-96-1P
294623-00-0P 294623-01-1P 294623-02-2P
294623-03-3P 294623-08-8P 294623-11-3P
294623-46-4P 294623-48-6P 361519-31-5P
361519-35-9P 361519-46-2P 361519-55-3P
361519-56-4P 361519-57-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-thiazolylbenzoyl-N-cyanomethyl-L-leucinamides and analogs as cysteine protease inhibitors for treatment of osteoporosis)

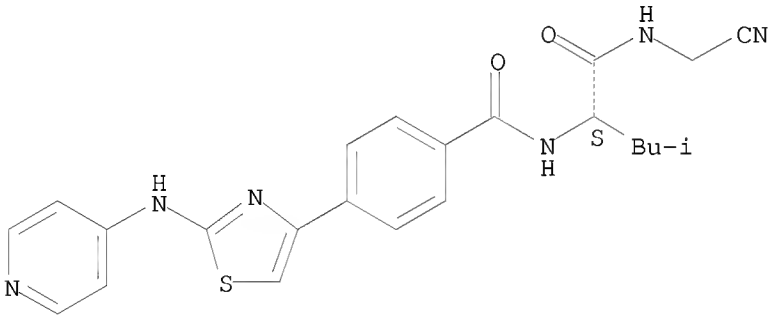
RN 294622-67-6 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methyl-3-buten-1-yl]-4-[2-(3-pyridinyl)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



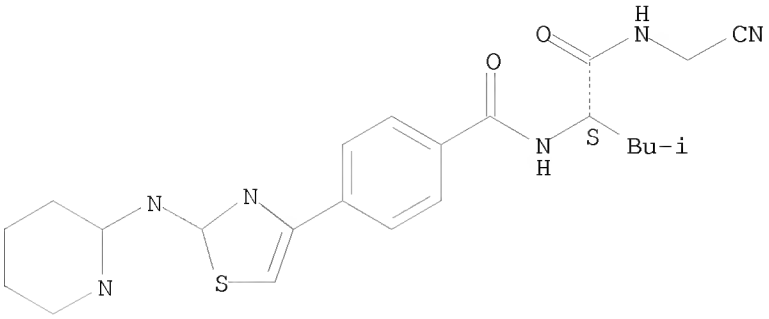
RN 294622-73-4 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[2-(4-pyridinylamino)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



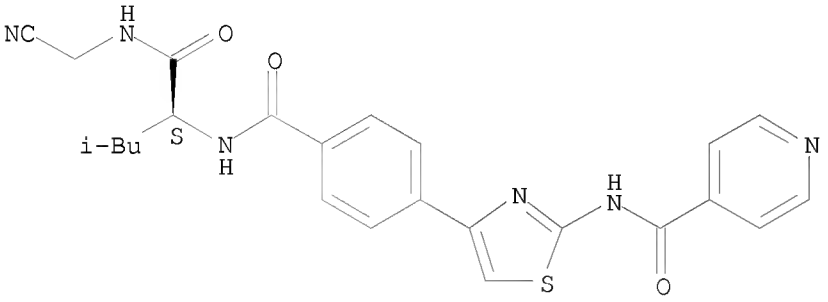
RN 294622-74-5 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[2-(2-pyridinylamino)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



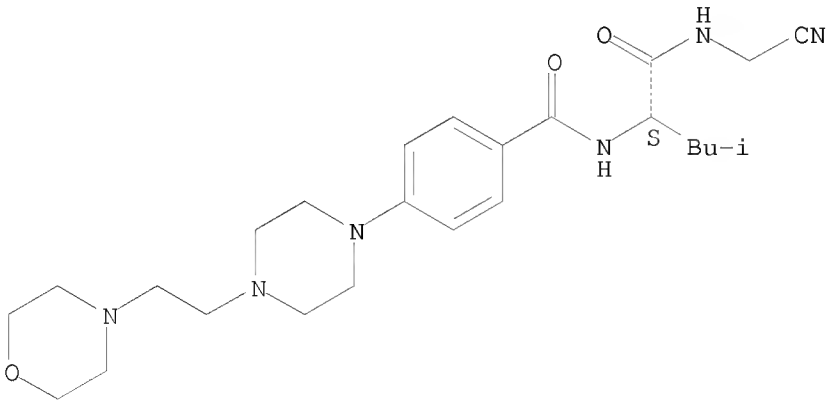
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 294622-75-6 CAPLUS
CN 4-Pyridinecarboxamide, N-[4-[4-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 294622-76-7 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[4-[2-(4-morpholinyl)ethyl]-1-piperazinyl]- (CA INDEX NAME)

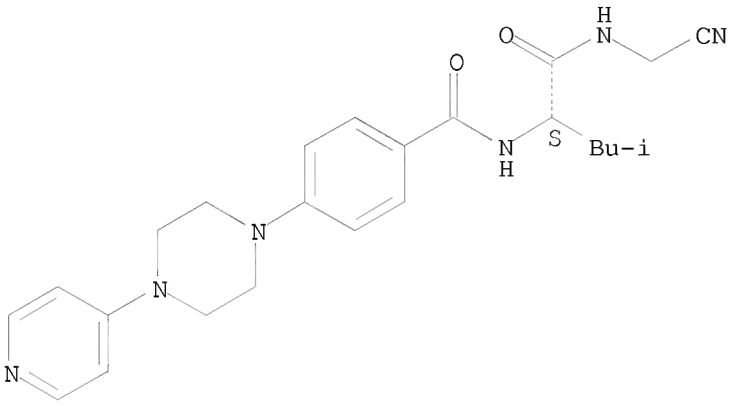
Absolute stereochemistry.



RN 294622-77-8 CAPLUS

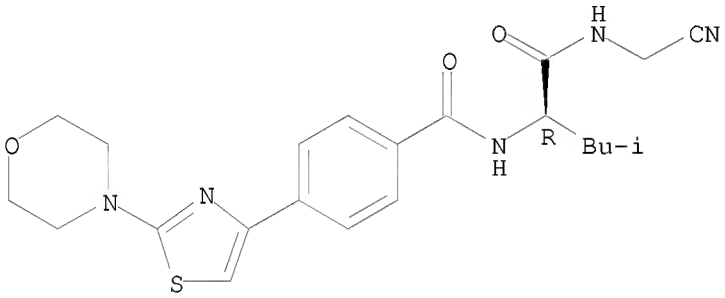
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[4-(4-pyridinyl)-1-piperazinyl]- (CA INDEX NAME)

Absolute stereochemistry.



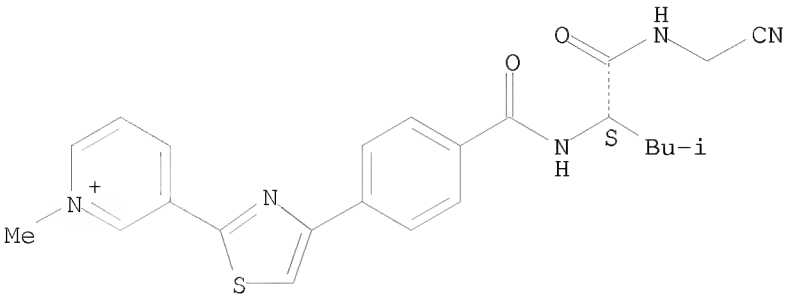
RN 294622-79-0 CAPLUS
CN Benzamide, N-[(1R)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[2-(4-morpholinyl)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 294622-82-5 CAPLUS
CN Pyridinium, 3-[4-[4-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]-1-methyl-, iodide (1:1) (CA INDEX NAME)

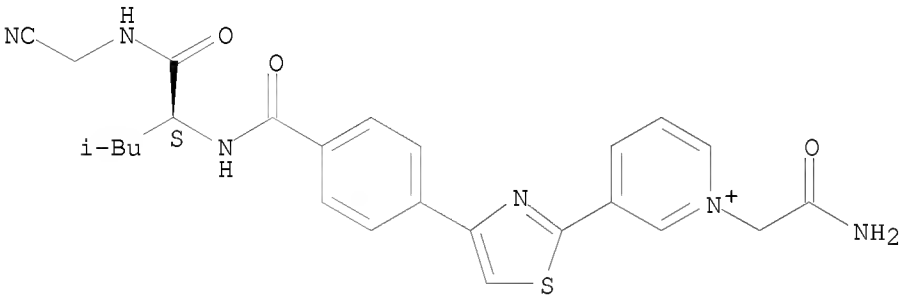
Absolute stereochemistry.



● I^-

RN 294622-83-6 CAPLUS
CN Pyridinium, 1-(2-amino-2-oxoethyl)-3-[4-[4-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]-, bromide (1:1) (CA INDEX NAME)

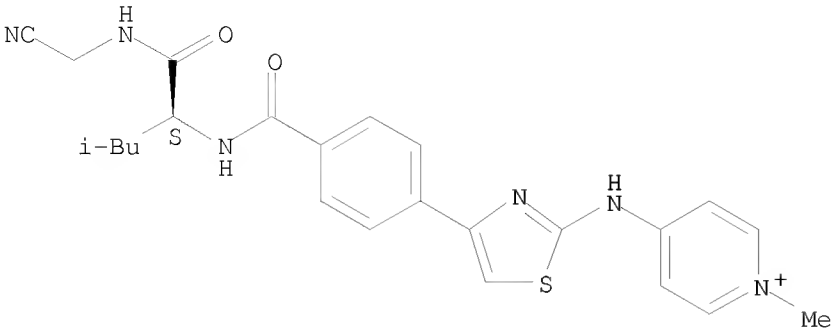
Absolute stereochemistry.



● Br^-

RN 294622-84-7 CAPLUS
CN Pyridinium, 4-[[4-[4-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]amino]-1-methyl-, iodide (1:1) (CA INDEX NAME)

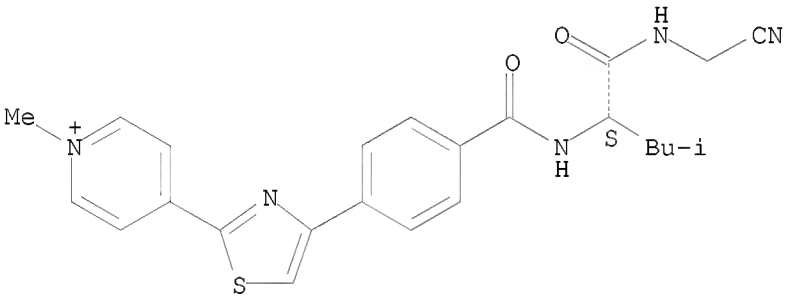
Absolute stereochemistry.



● I^-

RN 294622-85-8 CAPLUS
CN Pyridinium, 4-[4-[4-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]-1-methyl-, iodide (1:1) (CA INDEX NAME)

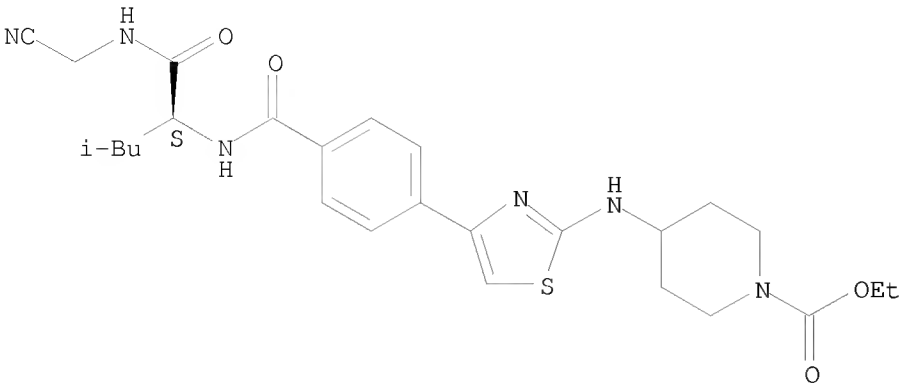
Absolute stereochemistry.



● I^-

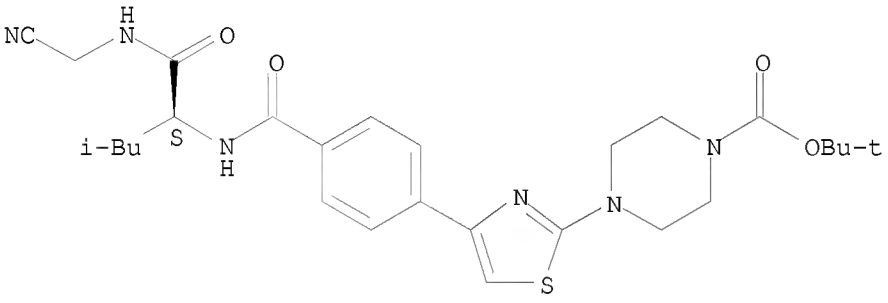
RN 294622-86-9 CAPLUS
CN 1-Piperidinecarboxylic acid, 4-[[4-[4-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]amino]-, ethyl ester (CA INDEX NAME)

Absolute stereochemistry.



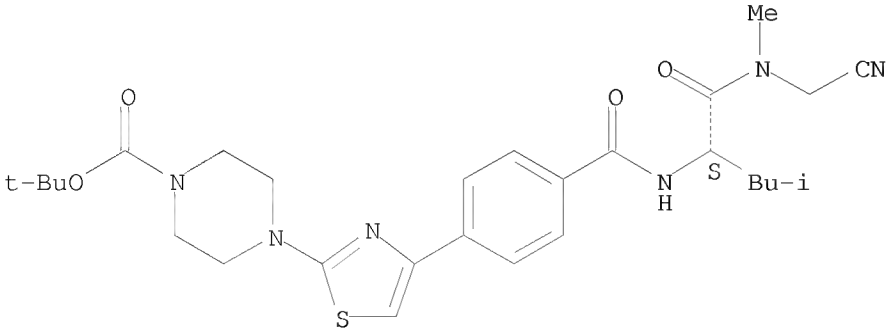
RN 294622-89-2 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-[4-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)

Absolute stereochemistry.



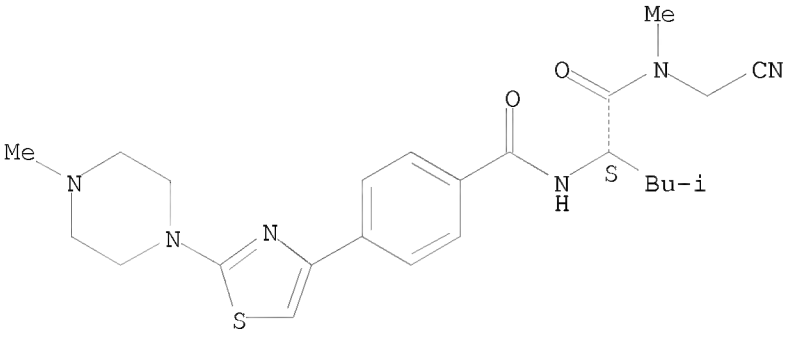
RN 294622-95-0 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-[4-[[[(1S)-1-[[(cyanomethyl)methylamino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)

Absolute stereochemistry.



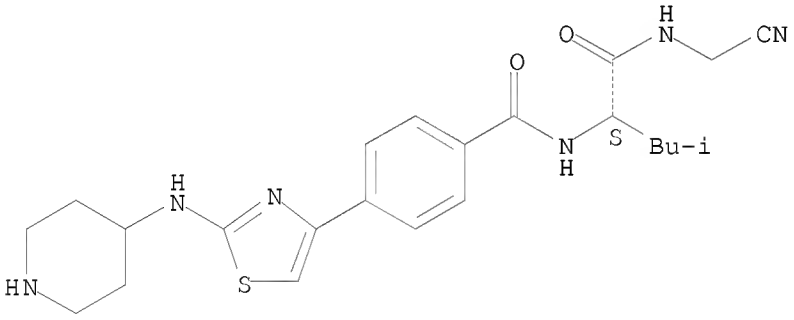
RN 294622-96-1 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)methylamino]carbonyl]-3-methylbutyl]-4-[2-(4-methyl-1-piperazinyl)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 294623-00-0 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[2-(4-piperidinylamino)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.

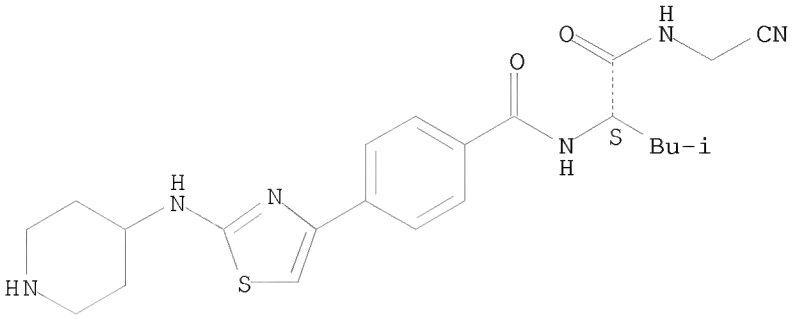


RN 294623-01-1 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[2-(4-piperidinylamino)-4-thiazolyl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

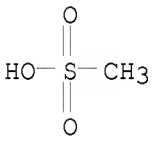
CRN 294623-00-0
CMF C23 H30 N6 O2 S

Absolute stereochemistry.



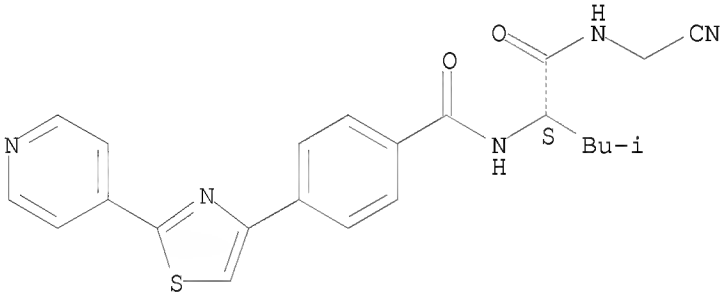
CM 2

CRN 75-75-2
CMF C H4 O3 S



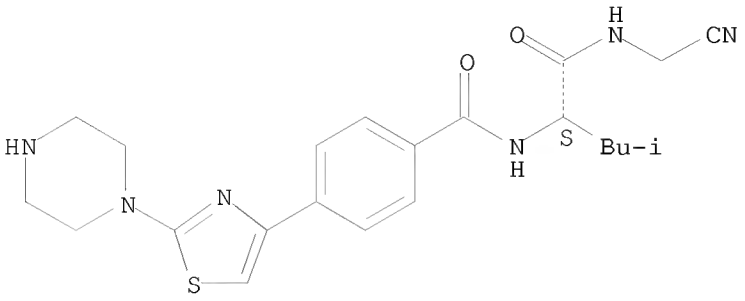
RN 294623-02-2 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[2-(4-pyridinyl)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



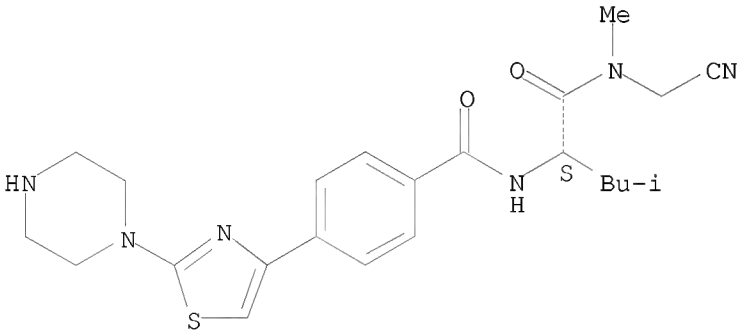
RN 294623-03-3 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[2-(1-piperazinyl)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



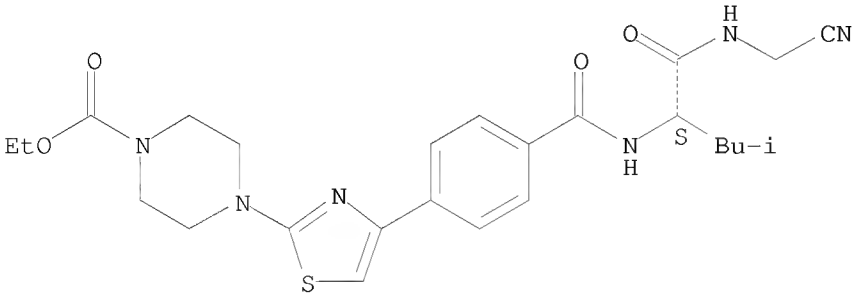
RN 294623-08-8 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)methylamino]carbonyl]-3-methylbutyl]-4-[2-(1-piperazinyl)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



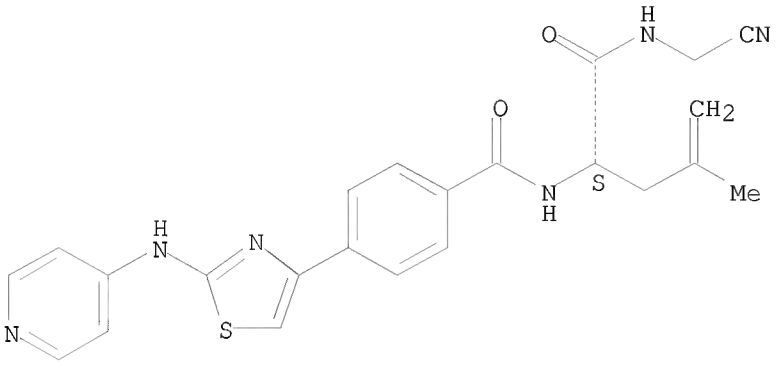
RN 294623-11-3 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-[4-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]-, ethyl ester (CA INDEX NAME)

Absolute stereochemistry.



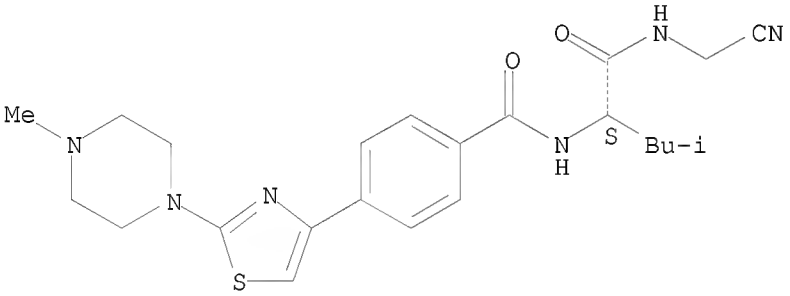
RN 294623-46-4 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methyl-3-buten-1-yl]-4-[2-(4-pyridinylamino)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



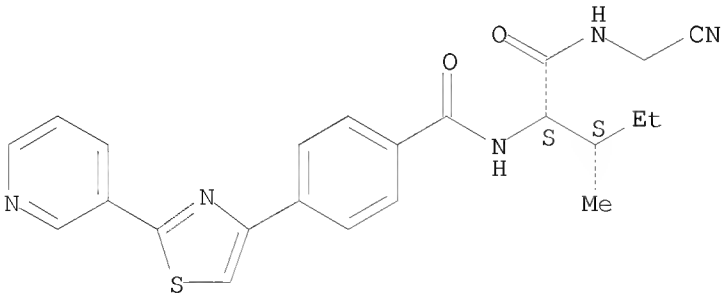
RN 294623-48-6 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[2-(4-methyl-1-piperazinyl)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 361519-31-5 CAPLUS
CN Benzamide, N-[(1S,2S)-1-[[(cyanomethyl)amino]carbonyl]-2-methylbutyl]-4-[2-(3-pyridinyl)-4-thiazolyl]- (CA INDEX NAME)

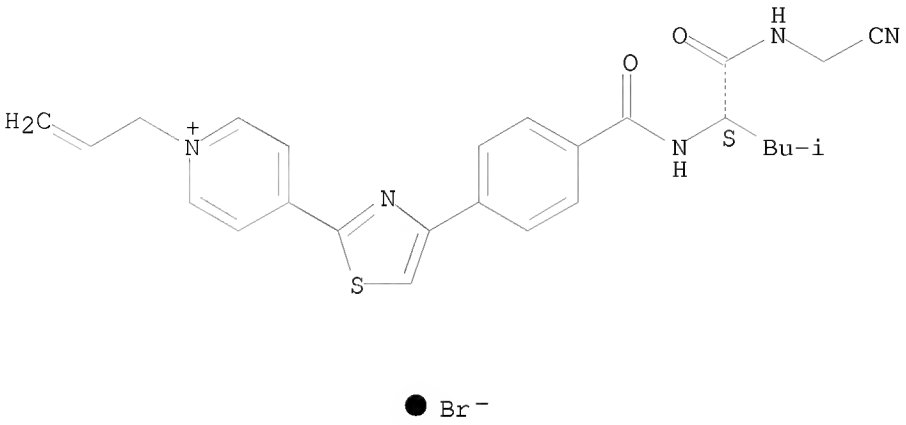
Absolute stereochemistry.



RN 361519-35-9 CAPLUS
CN Pyridinium, 4-[4-[4-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-

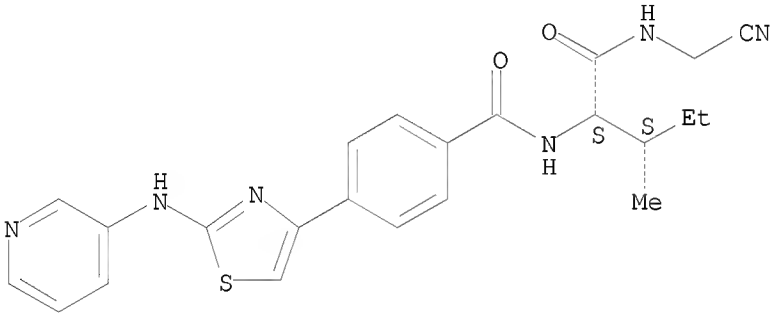
methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]-1-(2-propen-1-yl)-, bromide (1:1) (CA INDEX NAME)

Absolute stereochemistry.



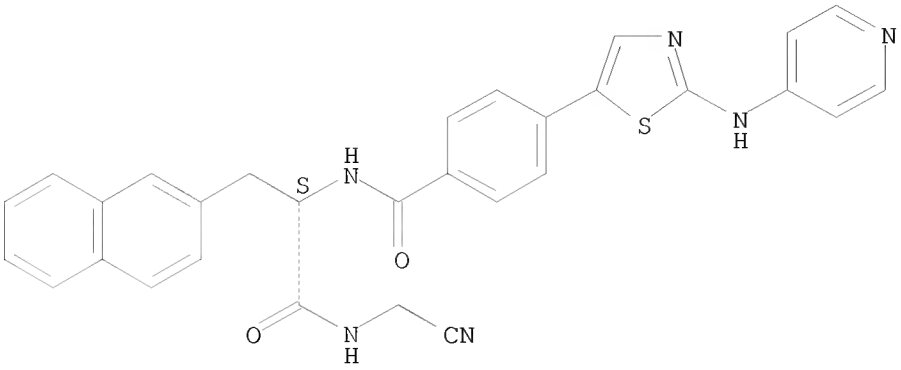
RN 361519-46-2 CAPLUS
CN Benzamide, N-[(1S,2S)-1-[[(cyanomethyl)amino]carbonyl]-2-methylbutyl]-4-[2-(3-pyridinylamino)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



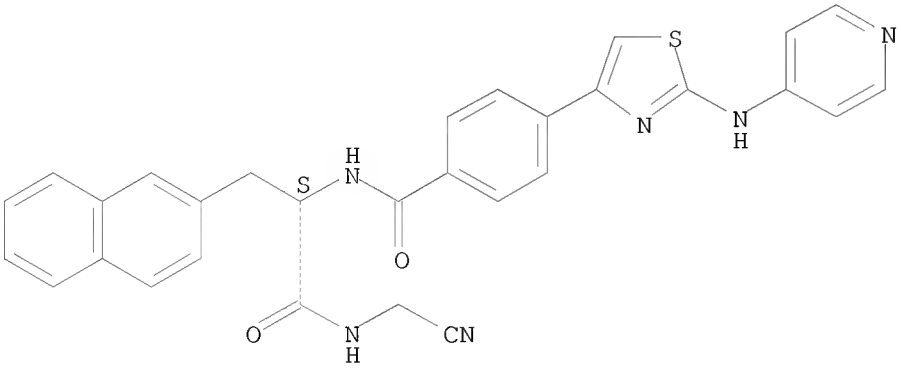
RN 361519-55-3 CAPLUS
CN 2-Naphthalenepropanamide, N-(cyanomethyl)-α-[[4-[2-(4-pyridinylamino)-5-thiazolyl]benzoyl]amino]-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.

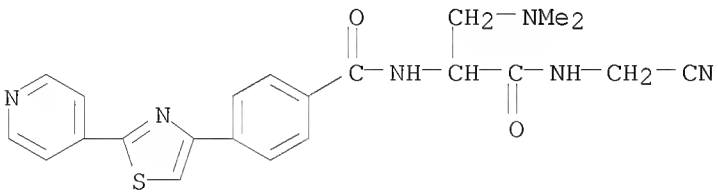


RN 361519-56-4 CAPLUS
CN 2-Naphthalenepropanamide, N-(cyanomethyl)-α-[[4-[2-(4-pyridinylamino)-4-thiazolyl]benzoyl]amino]-, (αS)- (CA INDEX NAME)

Absolute stereochemistry.



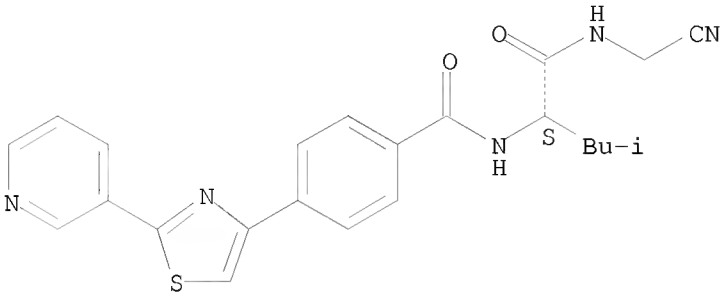
RN 361519-57-5 CAPLUS
CN Benzamide, N-[2-[(cyanomethyl)amino]-1-[(dimethylamino)methyl]-2-oxoethyl]-4-[2-(4-pyridinyl)-4-thiazolyl]- (CA INDEX NAME)



IT 294622-72-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of N-thiazolylbenzoyl-N-cyanomethyl-L-leucinamides and analogs as cysteine protease inhibitors for treatment of osteoporosis)
RN 294622-72-3 CAPLUS

CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[2-(3-pyridinyl)-4-thiazolyl]- (CA INDEX NAME)

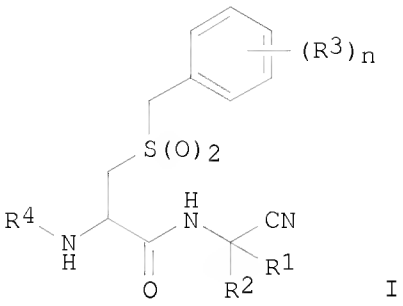
Absolute stereochemistry.



L4 ANSWER 34 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:208258 CAPLUS
DOCUMENT NUMBER: 134:237310
TITLE: Preparation and use of 2-aminoacyl-3-benzylsulfonylpropionamide derivatives as as cathepsin S inhibitors
INVENTOR(S): Graupe, Michael; Link, John O.; Patterson, John W.; Zipfel, Sheila
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001019808	A1	20010322	WO 2000-US25341		20000915
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
US 6492362	B1	20021210	US 2000-663449		20000915
MX 2002PA02873	A	20020830	MX 2002-PA2873		20020314
US 20040014796	A1	20040122	US 2002-256354		20020927
PRIORITY APPLN. INFO.:			US 1999-154245P	P	19990916
			US 1999-171831P	P	19991222
			US 2000-224552P	P	20000810
			US 2000-663449	A3	20000915
			WO 2000-US25418	W	20000915

OTHER SOURCE(S): MARPAT 134:237310
GI



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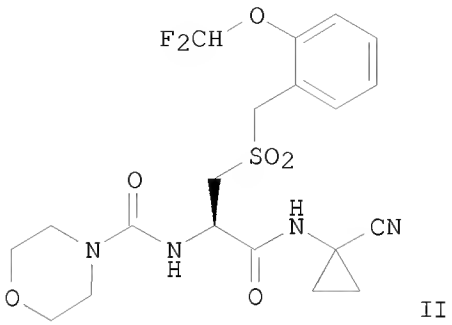


II

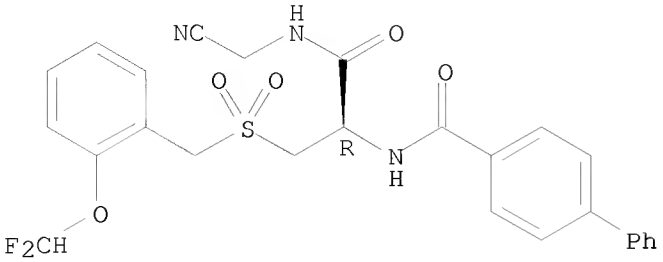
AB Compds. of formula I are claimed [wherein; n is 1-5, R1 is H and R2 is cyano, C5-heteroaryl or R1 and R2 are H, halo, alkyl, alkyl, X1OR5 where X1 and R5 are defined below or R1 and R2 together with the carbon atom, are (hetero)cycloalkylene; R3 is, at the first occurrence, NO2, CF3O, CHF2O, X1NR5R5, X1C(O)NR5R5, X1SR5, etc., where X1 is a bond or alkylene, R5 is H or (substituted)alkyl; R3 is at each other occurrence, is H, alkyl, CN, halo, etc.; R4 is C(O)X2R8 or S(O)2X2R8, where X2 is a bond, O or N(H or alkyl) and R8 is (substituted)alkyl, (hetero)cycloalkyl, substituted heteroaryl, etc.]. Preparation of I proceeds by one of four routes. The cyanomethyl amide side-chain may be formed by condensation of a cyanomethylamine with the parent carboxylic acid (optionally as the sulfide analog, followed by oxidation to the sulfone). The R4-NH bond may be formed by alkylation of the parent amine salt with R4L where L is a leaving group, or by addition of an amine to the corresponding isocyanate. Alternatively, the thiol-derived parent may be S-benzylated and oxidized to give compds. I. Compound II was prepared by amidation of (R)-3-[2-(difluoromethoxy)benzylsulfonyl]-2-[(1-morpholin-4-ylmethanoyl)amino]propionic acid with (1-aminocyclopropane)carbonitrile. Seventy examples of compds. I were provided. I showed Ki against cathepsin S activity in the range of 10-10 to 10-7 M. I inhibited cathepsin K 50-fold less than cathepsin S. Claimed uses of I are treatment of diseases which inhibition of cathepsin S can prevent.

IT 330475-22-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and use of 2-aminoacyl-3-benzylsulfonylpropionamide derivs. as selective cathepsin S inhibitors)

RN 330475-22-4 CAPLUS

CN [1,1'-Biphenyl]-4-carboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[[2-(difluoromethoxy)phenyl]methyl]sulfonyl]methyl]-2-oxoethyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 35 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:208246 CAPLUS
DOCUMENT NUMBER: 134:237830
TITLE: Preparation of amino acid cyanomethyl amides as cathepsin S inhibitors
INVENTOR(S): Graupe, Michael; Link, John O.; Patterson, John W.; Zipfel, Sheila
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 261 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001019796	A1	20010322	WO 2000-US25415		20000915
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2384974	A1	20010322	CA 2000-2384974		20000915
EP 1212302	A1	20020612	EP 2000-966734		20000915
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
US 6492362	B1	20021210	US 2000-663449		20000915
JP 2003509410	T	20030311	JP 2001-523376		20000915
AU 777472	B2	20041021	AU 2000-77033		20000915
MX 2002PA02873	A	20020830	MX 2002-PA2873		20020314
US 20040014796	A1	20040122	US 2002-256354		20020927
PRIORITY APPLN. INFO.:			US 1999-154245P	P	19990916
			US 1999-171831P	P	19991222
			US 2000-224552P	P	20000810
			US 2000-663449	A3	20000915
			WO 2000-US25415	W	20000915
			WO 2000-US25418	W	20000915

OTHER SOURCE(S): MARPAT 134:237830

AB R4NHCH(X1SO2X2R3)CONHCR1R2CN [X1, X2 = CH2, or X1 = CH2CH2 and X2 = bond; R1 = H, R2 = cyano, heteroaryl, alkylheteroaryl, or R1, R2 = H, halo, alkyl, X3OR9; R1R2C = cycloalkylene, heterocycloalkylene; R3 = (substituted) CHR5:CHR6, CR7:NR8; R5R6 = atoms to form alkenyl, cycloalkenyl, heterocycloalkenyl, aryl, heteroaryl, etc.; R7R8 = atoms to form heterocycloalkenyl, heteroaryl, heterobicycloaryl; R4 = COX4R11, SO2X4R11; X4 = bond, O, NR12; R12 = H, alkyl; R11 = (substituted) alkyl, cycloalkylalkyl, heterocycloalkylalkyl, etc.; R9 = H, alkyl, haloalkyl; X3 = bond, alkylene], were prepared Thus, 2R-benzoylamino-3-(4-methylbenzylsulfanyl)propionic acid (preparation given), EDCI, HOBt, aminoacetonitrile bisulfate, and N-methylmorpholine were stirred together in N-methylpyrrolidinone for 5 h to give N-[1R-cyanomethylcarbamoyl-2-(4-methylbenzylsulfanyl)ethyl]benzamide. This was stirred with oxone in MeOH for 16 h to give N-[(R)-1-(cyanomethylcarbamoyl)-2-p-tolylmethanesulfonylethyl]benzamide. Title compds. inhibited cathepsin S with Ki = about 10-10 M to 10-4 M.

IT 330473-99-9P 330475-22-4P

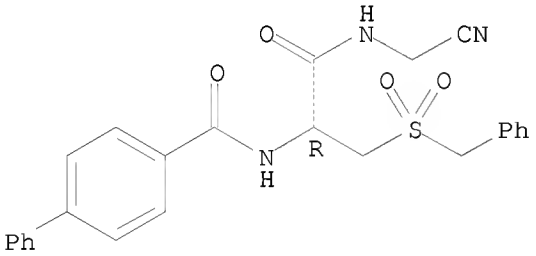
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amino acid cyanomethyl amides as cathepsin S inhibitors)

RN 330473-99-9 CAPLUS

CN [1,1'-Biphenyl]-4-carboxamide, N-[(1R)-2-[(cyanomethyl)amino]-2-oxo-1-[[(phenylmethyl)sulfonyl]methyl]ethyl]- (CA INDEX NAME)

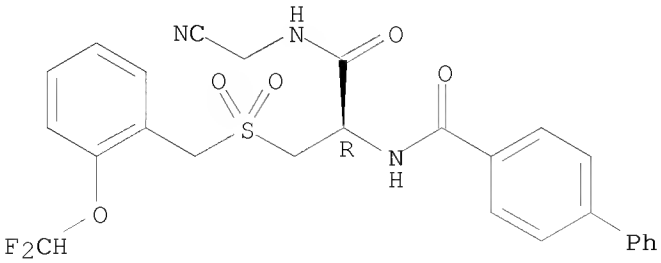
Absolute stereochemistry.



RN 330475-22-4 CAPLUS

CN [1,1'-Biphenyl]-4-carboxamide, N-[(1R)-2-[(cyanomethyl)amino]-1-[[[[2-(difluoromethoxy)phenyl]methyl]sulfonyl]methyl]-2-oxoethyl]- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 36 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:666701 CAPLUS
DOCUMENT NUMBER: 133:252050
TITLE: Preparation of novel N-cyanomethyl amide compounds and compositions as protease inhibitors to treat osteoporosis
INVENTOR(S): Bryant, Clifford M.; Palmer, James T.; Rydzewski, Robert M.; Setti, Eduardo L.; Tian, Zong-Qiang; Venkatraman, Shankar; Wang, Dan-Xiong
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 155 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000055126	A2	20000921	WO 2000-US6837	20000315
WO 2000055126	A3	20010222		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2368148	A1	20000921	CA 2000-2368148	20000315
EP 1161415	A2	20011212	EP 2000-916375	20000315
EP 1161415	B1	20050713		
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TR 200103337	T2	20020321	TR 2001-3337	20000315
TR 200103390	T2	20020521	TR 2001-3390	20000315
HU 2002000347	A2	20020629	HU 2002-347	20000315
HU 2002000347	A3	20030528		
HU 2002000503	A2	20020629	HU 2002-503	20000315
HU 2002000503	A3	20050628		
US 6455502	B1	20020924	US 2000-526090	20000315
TR 200201874	T2	20021021	TR 2002-1874	20000315
US 6476026	B1	20021105	US 2000-526485	20000315
JP 2002539192	T	20021119	JP 2000-605557	20000315
EE 200100487	A	20030217	EE 2001-487	20000315
AU 769736	B2	20040205	AU 2000-37486	20000315
PT 1178958	T	20040730	PT 2000-916343	20000315
EP 1452522	A2	20040901	EP 2004-75486	20000315
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AT 299493	T	20050715	AT 2000-916375	20000315

ES 2245303	T3	20060101	ES 2000-916375		20000315
TW 290132	B	20071121	TW 2000-89104606		20010605
ZA 2001007494	A	20020911	ZA 2001-7494		20010911
ZA 2001007495	A	20020911	ZA 2001-7495		20010911
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BG 106013	A	20020531	BG 2001-106013		20011012
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US 6593327	B2	20030715			
US 20030096796	A1	20030522	US 2002-205600		20020724
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US 20040147745	A1	20040729	US 2004-758893		20040115
US 20070015755	A1	20070118	US 2006-533582		20060920
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			EP 2000-916343	A3	20000315
			US 2000-526090	A1	20000315
			US 2000-526485	A3	20000315
			WO 2000-US6837	W	20000315
			US 2002-205600	B1	20020724
			US 2004-758893	B1	20040115

OTHER SOURCE(S): MARPAT 133:252050

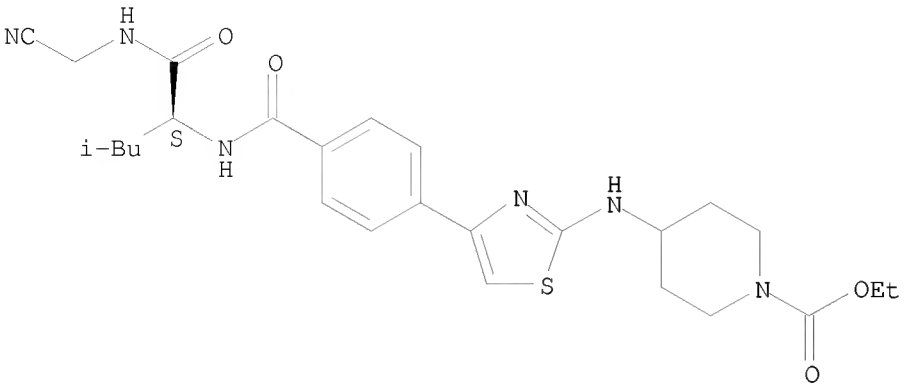
AB Title compds. [R1R2NCR3R4CN; R1 = R11R7NCR5R9X1, R11R8NCR6R10X2NR7CR5R9CX1; X1, X2 independently = CO, CH2SO2; R5, R6 independently = H, C1-6alkyl; R7, R8 independently = H, C1-6alkyl; R9, R10 independently = (un)substituted-C1-6alkyl; R9-R7 = trimethylene, tetramethylene, phenylene-1,2-dimethylene; R10-R8 = trimethylene, tetramethylene, phenylene-1,2-dimethylene; R5-R9 = C3-8cycloalkylene, C3-8heterocycloalkylene; R10-R6 = C3-8cycloalkylene, C3-8heterocycloalkylene; R11 = X4X5R18; X4 = CO, COCO, SO2; X5 = bond, O, NH; R18 = C1-6alkyl; R2 = H, C1-6alkyl; R3 = H, C1-6alkyl; R4 = CN, COOH, COOC1-6alkyl; R2-R4 = trimethylene, tetramethylene, phenylene-1,2-dimethylene; R4-R3 = C3-8cycloalkylene, C3-8heterocycloalkylene], N-oxide, prodrug, isomers, pharmaceutically acceptable salts, and composition are prepared as therapeutically effective estrogen receptor agonist. Title compds. are claimed in treating osteoporosis in post-menopausal woman in which cathepsin K activity contributes to the pathol. and symptomatol. of the disease. Thus, the title compound (S)-C6H5CH2OCONHCH(CH2CH(CH3)2)CONHCH2CN was prepared

IT 294622-86-9P 294623-01-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of novel N-cyanomethyl amides and compns. as protease inhibitors)

RN 294622-86-9 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[4-[4-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]amino]-, ethyl ester (CA INDEX NAME)

Absolute stereochemistry.

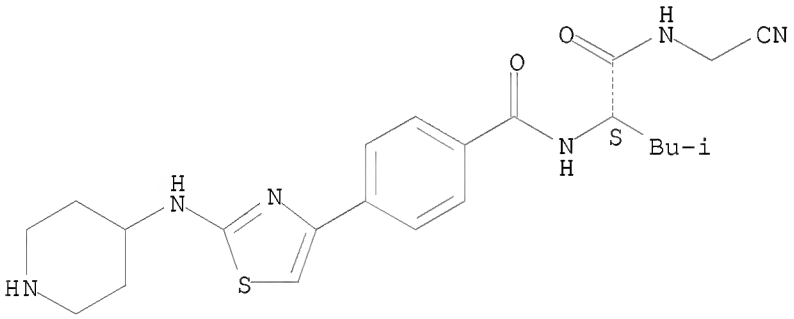


RN 294623-01-1 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[2-(4-piperidinylamino)-4-thiazolyl]-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

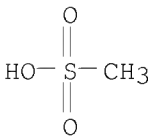
CRN 294623-00-0
CMF C23 H30 N6 O2 S

Absolute stereochemistry.



CM 2

CRN 75-75-2
CMF C H4 O3 S



IT 294620-34-1P 294620-43-2P 294620-45-4P
294620-46-5P 294620-47-6P 294620-48-7P

294620-49-8P 294620-50-1P 294620-51-2P
294620-52-3P 294620-53-4P 294620-58-9P
294620-91-0P 294620-98-7P 294621-00-4P
294621-01-5P 294621-02-6P 294621-03-7P
294621-07-1P 294621-13-9P 294621-14-0P
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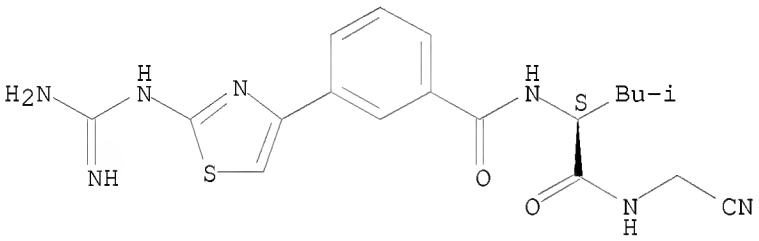
294623-40-8P 294623-42-0P 294623-44-2P
294623-45-3P 294623-46-4P 294623-47-5P
294623-48-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel N-cyanomethyl amides and compns. as protease inhibitors)

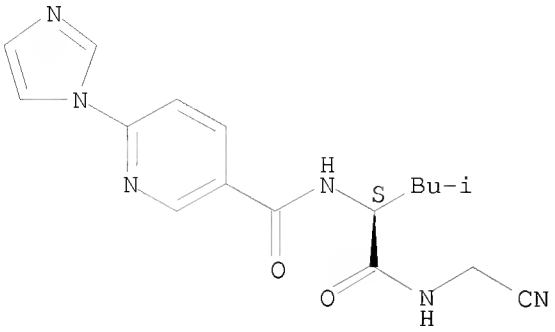
RN 294620-34-1 CAPLUS
CN Benzamide, 3-[2-[(aminoiminomethyl)amino]-4-thiazolyl]-N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]- (CA INDEX NAME)

Absolute stereochemistry.



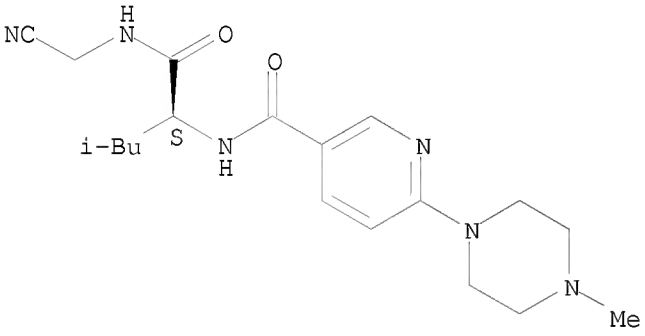
RN 294620-43-2 CAPLUS
CN 3-Pyridinecarboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-6-(1H-imidazol-1-yl)- (CA INDEX NAME)

Absolute stereochemistry.



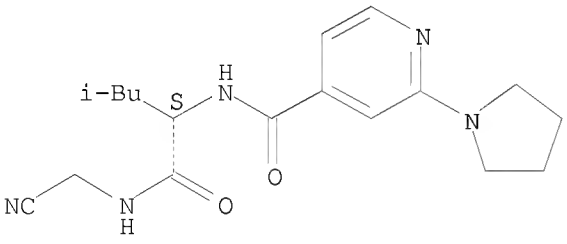
RN 294620-45-4 CAPLUS
CN 3-Pyridinecarboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-6-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

Absolute stereochemistry.



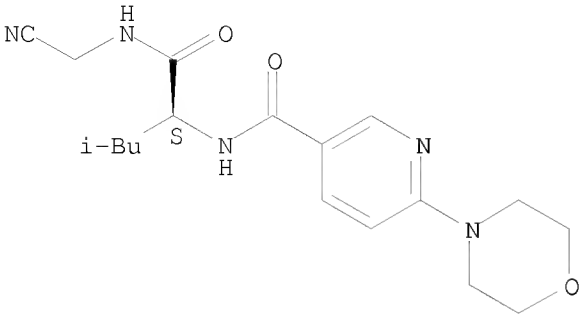
RN 294620-46-5 CAPLUS
CN 4-Pyridinecarboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-2-(1-pyrrolidinyl)- (CA INDEX NAME)

Absolute stereochemistry.



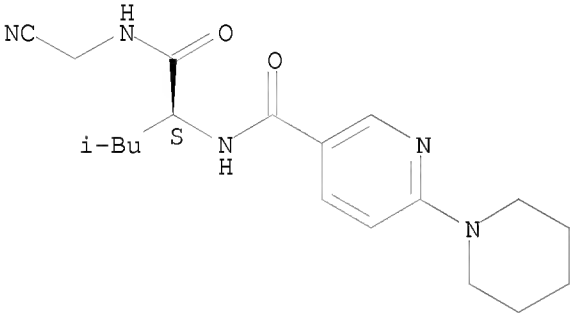
RN 294620-47-6 CAPLUS
CN 3-Pyridinecarboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-6-(4-morpholinyl)- (CA INDEX NAME)

Absolute stereochemistry.



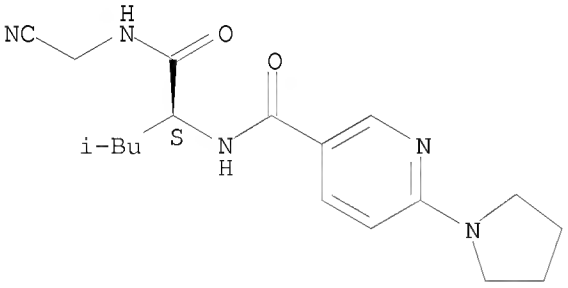
RN 294620-48-7 CAPLUS
CN 3-Pyridinecarboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-6-(1-piperidinyl)- (CA INDEX NAME)

Absolute stereochemistry.



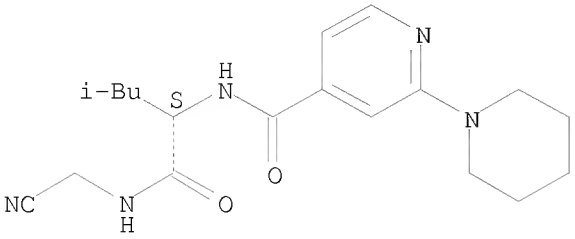
RN 294620-49-8 CAPLUS
CN 3-Pyridinecarboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-6-(1-pyrrolidinyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 294620-50-1 CAPLUS
CN 4-Pyridinecarboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-2-(1-piperidinyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 294620-51-2 CAPLUS
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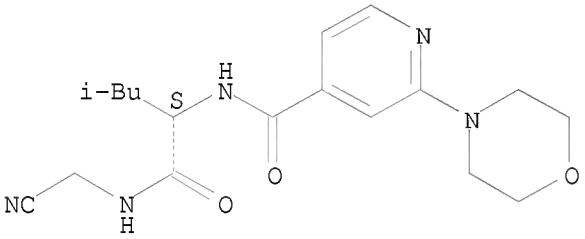
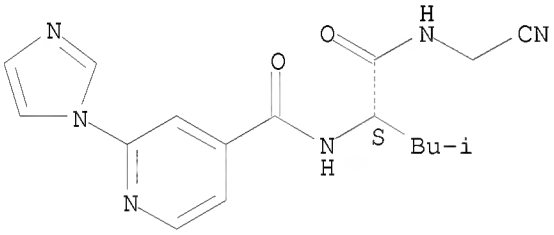
Absolute stereochemistry.



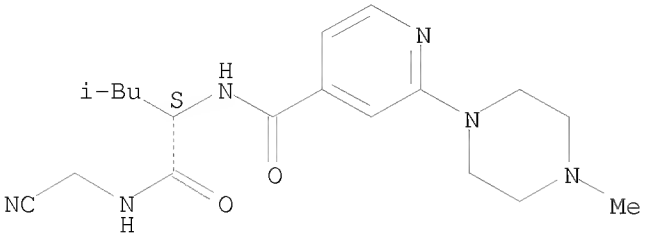
RN 294620-52-3 CAPLUS
CN 4-Pyridinecarboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-2-(1H-imidazol-1-yl)- (CA INDEX NAME)

Absolute stereochemistry.



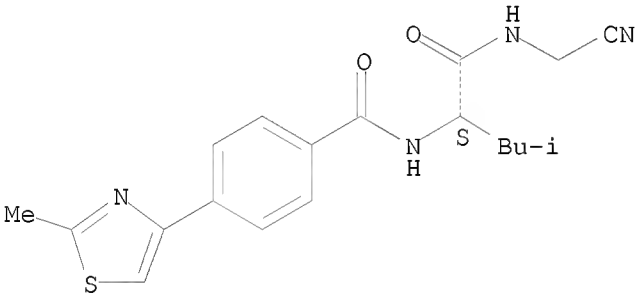
RN 294620-53-4 CAPLUS
CN 4-Pyridinecarboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-2-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

Absolute stereochemistry.



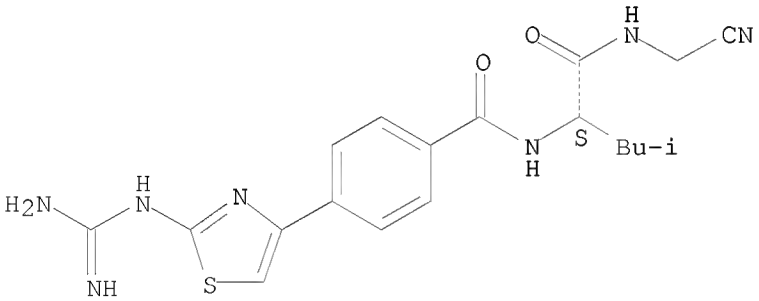
RN 294620-58-9 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-(2-methyl-4-thiazolyl)- (CA INDEX NAME)

Absolute stereochemistry.



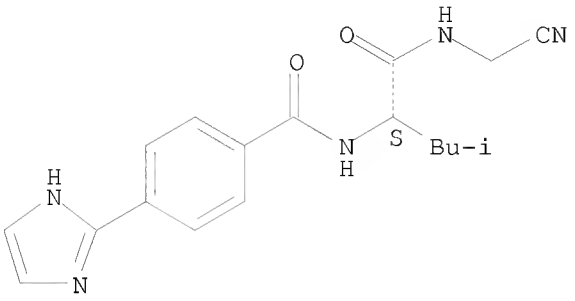
RN 294620-91-0 CAPLUS
CN Benzamide, 4-[2-[(aminoiminomethyl)amino]-4-thiazolyl]-N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]- (CA INDEX NAME)

Absolute stereochemistry.



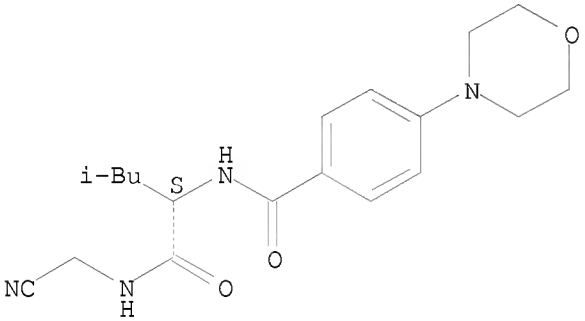
RN 294620-98-7 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-(1H-imidazol-2-yl)- (CA INDEX NAME)

Absolute stereochemistry.



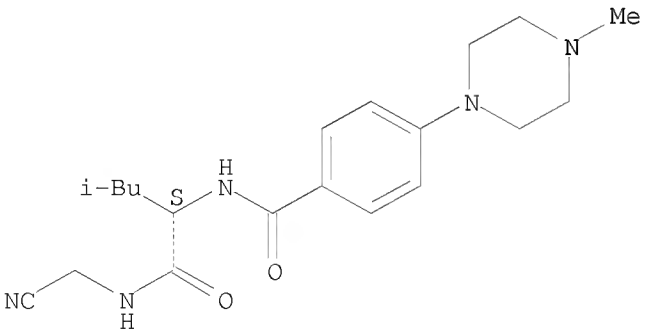
RN 294621-00-4 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-(4-morpholinyl)- (CA INDEX NAME)

Absolute stereochemistry.



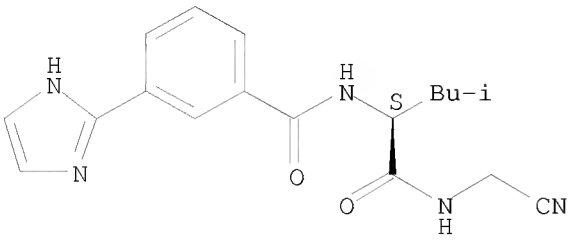
RN 294621-01-5 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)

Absolute stereochemistry.



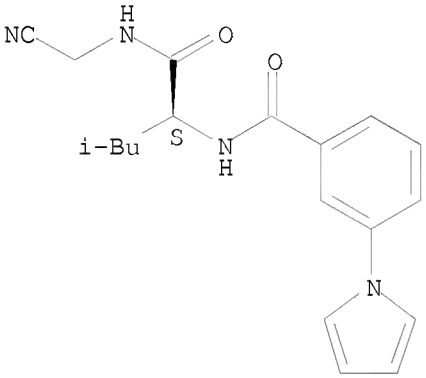
RN 294621-02-6 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-3-(1H-imidazol-2-yl)- (CA INDEX NAME)

Absolute stereochemistry.

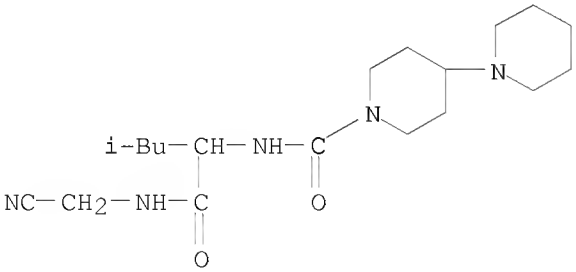


RN 294621-03-7 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-3-(1H-pyrrol-1-yl)- (CA INDEX NAME)

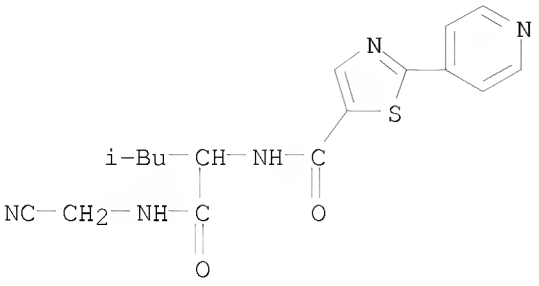
Absolute stereochemistry.



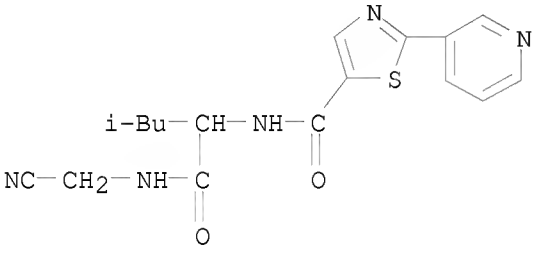
RN 294621-07-1 CAPLUS
CN [1,4'-Bipiperidine]-1'-carboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]- (CA INDEX NAME)



RN 294621-13-9 CAPLUS
CN 5-Thiazolecarboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-2-(4-pyridinyl)- (CA INDEX NAME)

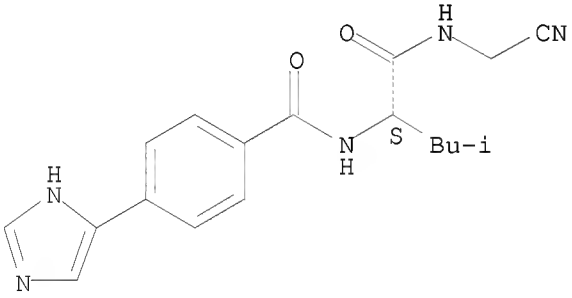


RN 294621-14-0 CAPLUS
CN 5-Thiazolecarboxamide, N-[1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-2-(3-pyridinyl)- (CA INDEX NAME)

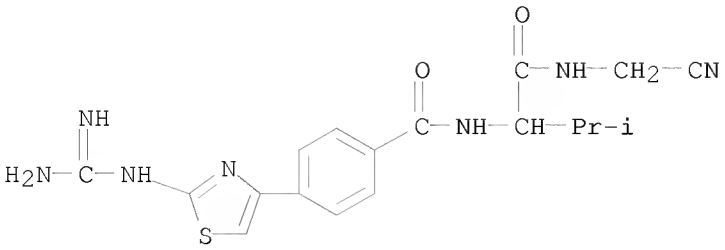


RN 294621-36-6 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-(1H-imidazol-5-yl)- (CA INDEX NAME)

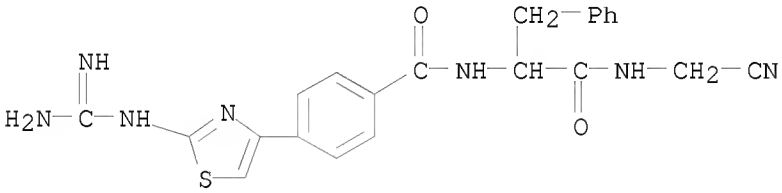
Absolute stereochemistry.



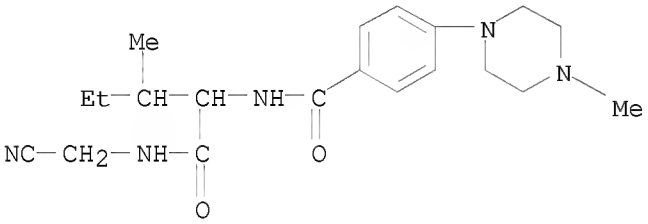
RN 294621-37-7 CAPLUS
CN Benzamide, 4-[2-[(aminoiminomethyl)amino]-4-thiazolyl]-N-[1-[[(cyanomethyl)amino]carbonyl]-2-methylpropyl]- (CA INDEX NAME)



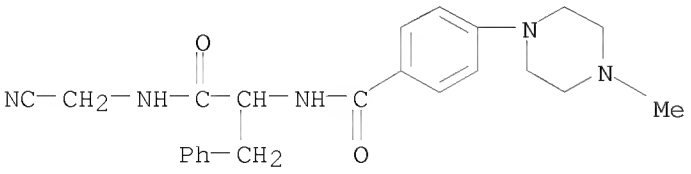
RN 294621-38-8 CAPLUS
CN Benzenepropanamide, α-[[4-[2-[(aminoiminomethyl)amino]-4-thiazolyl]benzoyl]amino]-N-(cyanomethyl)- (CA INDEX NAME)



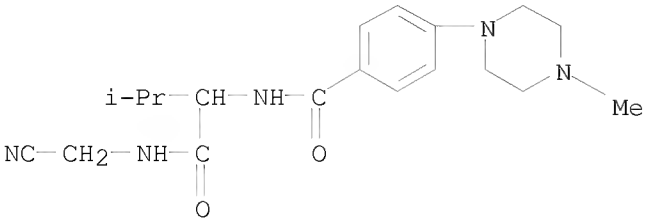
RN 294621-39-9 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]-2-methylbutyl]-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



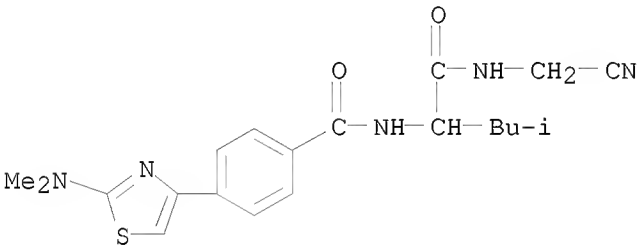
RN 294621-40-2 CAPLUS
CN Benzenepropanamide, N-(cyanomethyl)-α-[[4-(4-methyl-1-piperazinyl)benzoyl]amino]- (CA INDEX NAME)



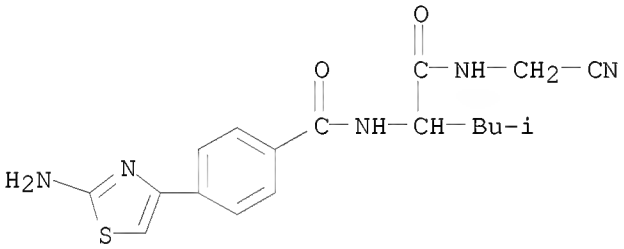
RN 294621-41-3 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]-2-methylpropyl]-4-(4-methyl-1-piperazinyl)- (CA INDEX NAME)



RN 294621-42-4 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[2-(dimethylamino)-4-thiazolyl]- (CA INDEX NAME)

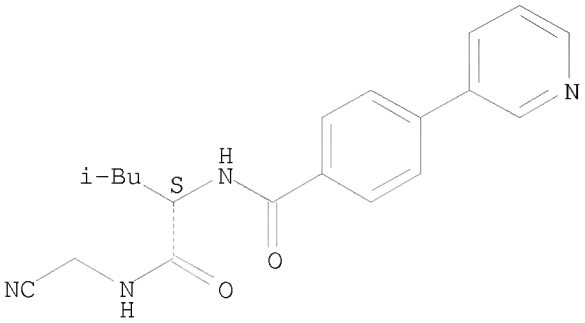


RN 294621-43-5 CAPLUS
CN Benzamide, 4-(2-amino-4-thiazolyl)-N-[1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]- (CA INDEX NAME)



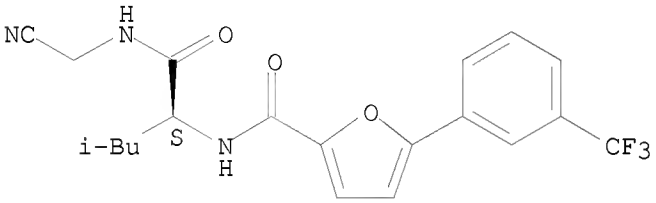
RN 294621-71-9 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-(3-pyridinyl)- (CA INDEX NAME)

Absolute stereochemistry.



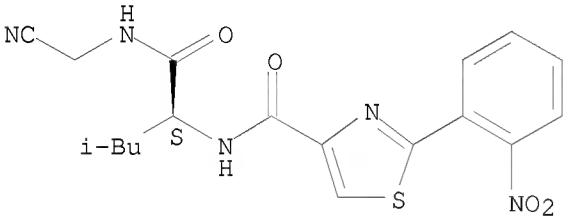
RN 294622-05-2 CAPLUS
CN 2-Furancarboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-5-[3-(trifluoromethyl)phenyl]- (CA INDEX NAME)

Absolute stereochemistry.



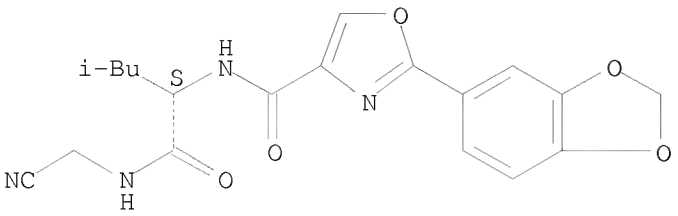
RN 294622-07-4 CAPLUS
CN 4-Thiazolecarboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-2-(2-nitrophenyl)- (CA INDEX NAME)

Absolute stereochemistry.



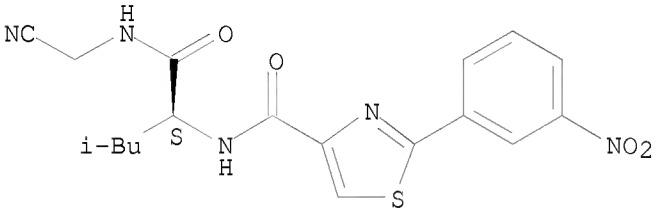
RN 294622-08-5 CAPLUS
CN 4-Oxazolecarboxamide, 2-(1,3-benzodioxol-5-yl)-N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]- (CA INDEX NAME)

Absolute stereochemistry.



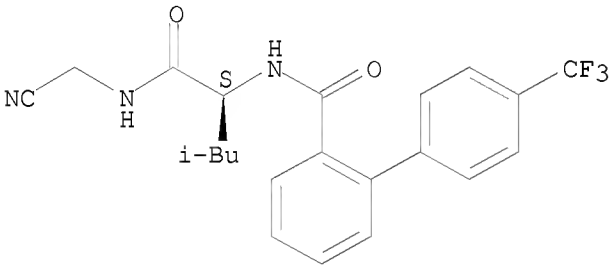
RN 294622-12-1 CAPLUS
CN 4-Thiazolecarboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-2-(3-nitrophenyl)- (CA INDEX NAME)

Absolute stereochemistry.



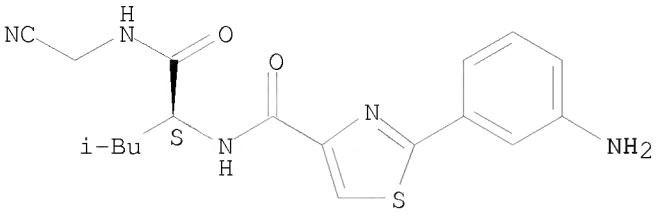
RN 294622-17-6 CAPLUS
CN [1,1'-Biphenyl]-2-carboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4'-(trifluoromethyl)- (CA INDEX NAME)

Absolute stereochemistry.



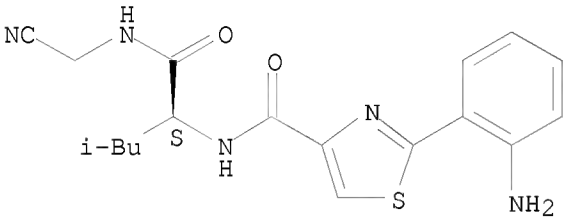
RN 294622-21-2 CAPLUS
CN 4-Thiazolecarboxamide, 2-(3-aminophenyl)-N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]- (CA INDEX NAME)

Absolute stereochemistry.



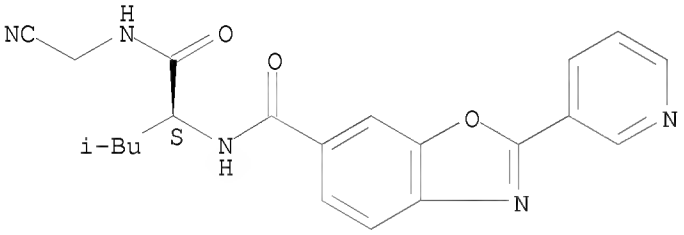
RN 294622-22-3 CAPLUS
CN 4-Thiazolecarboxamide, 2-(2-aminophenyl)-N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]- (CA INDEX NAME)

Absolute stereochemistry.



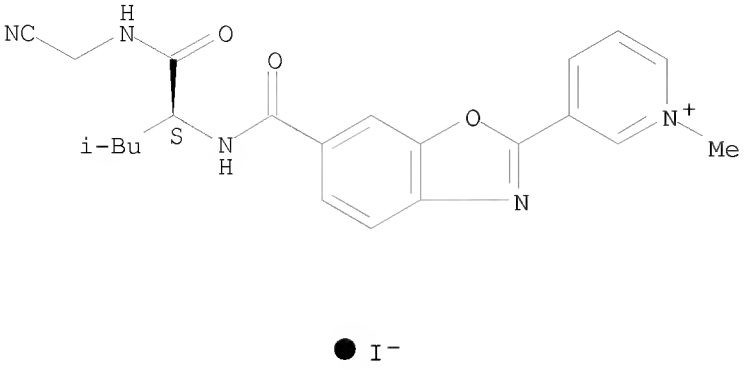
RN 294622-24-5 CAPLUS
CN 6-Benzoxazolecarboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-2-(3-pyridinyl)- (CA INDEX NAME)

Absolute stereochemistry.



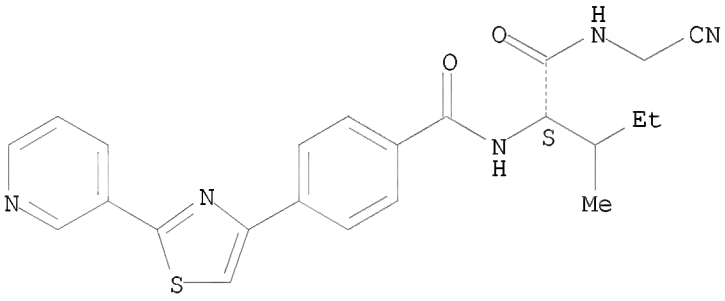
RN 294622-26-7 CAPLUS
CN Pyridinium, 3-[6-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]-2-benzoxazolyl]-1-methyl-, iodide (1:1) (CA INDEX NAME)

Absolute stereochemistry.



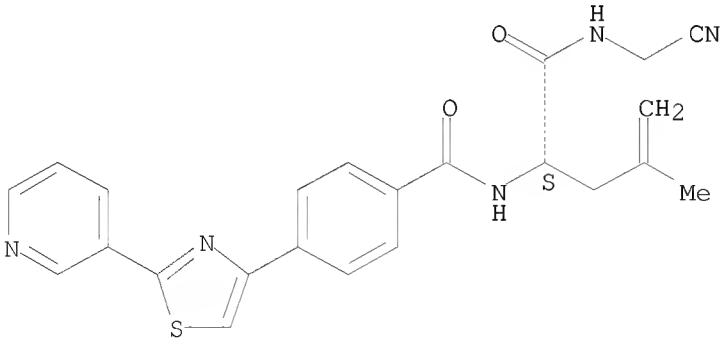
RN 294622-64-3 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-2-methylbutyl]-4-[2-(3-pyridinyl)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 294622-67-6 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methyl-3-buten-1-yl]-4-[2-(3-pyridinyl)-4-thiazolyl]- (CA INDEX NAME)

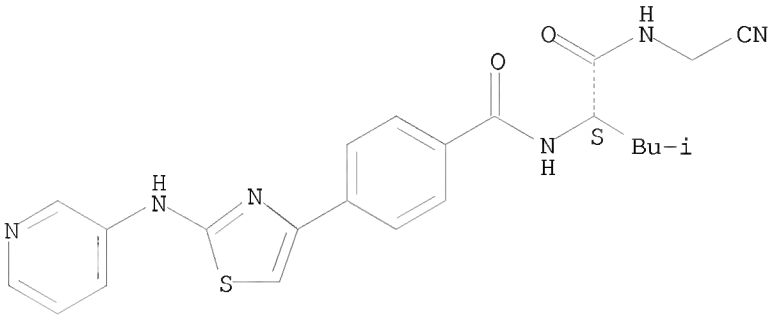
Absolute stereochemistry.



RN 294622-70-1 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[2-(3-

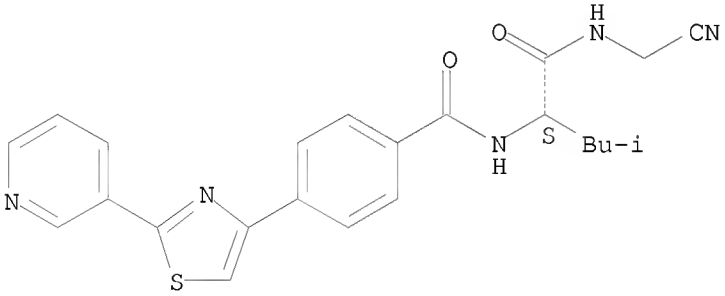
pyridinylamino)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



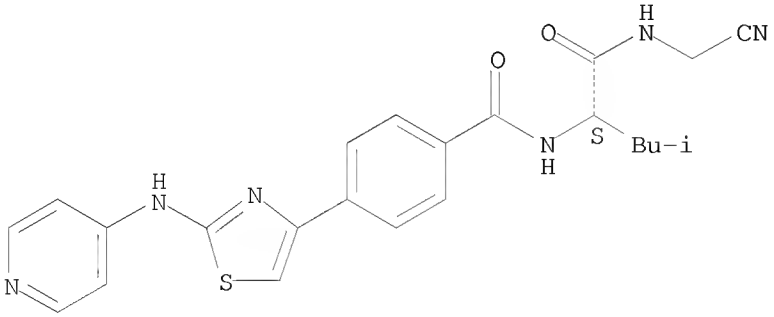
RN 294622-72-3 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[2-(3-pyridinyl)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



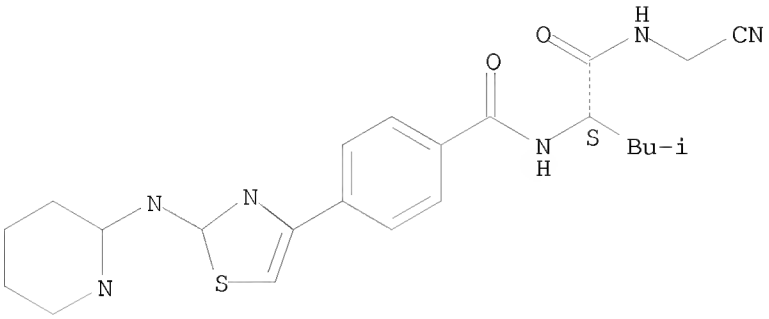
RN 294622-73-4 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[2-(4-pyridinylamino)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



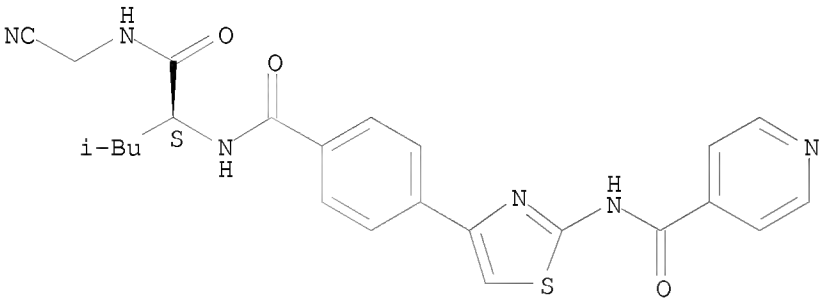
RN 294622-74-5 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[2-(2-pyridinylamino)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



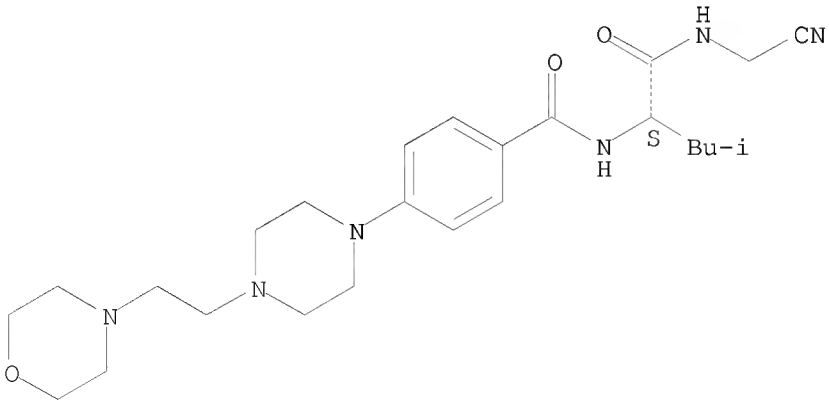
ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE
RN 294622-75-6 CAPLUS
CN 4-Pyridinecarboxamide, N-[4-[4-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



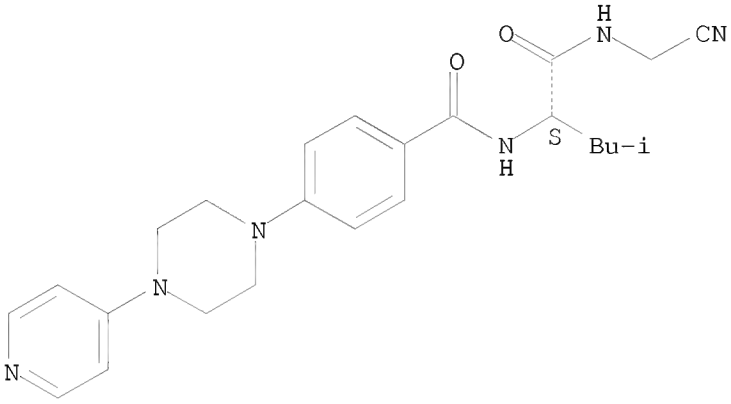
RN 294622-76-7 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[4-[2-(4-morpholinyl)ethyl]-1-piperazinyl]- (CA INDEX NAME)

Absolute stereochemistry.



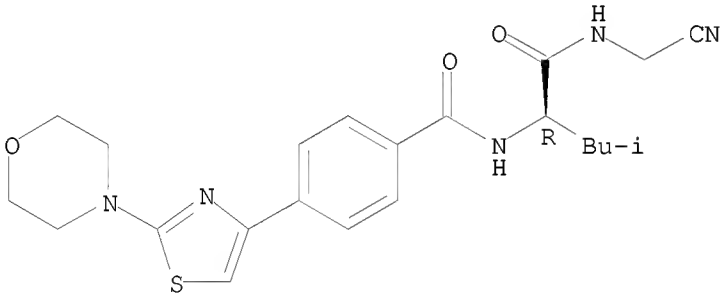
RN 294622-77-8 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[4-(4-pyridinyl)-1-piperazinyl]- (CA INDEX NAME)

Absolute stereochemistry.



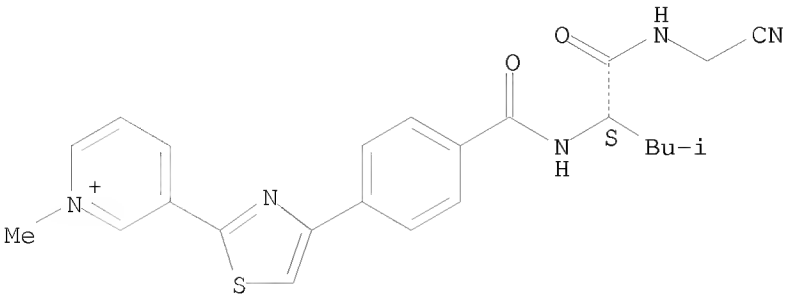
RN 294622-79-0 CAPLUS
CN Benzamide, N-[(1R)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[2-(4-morpholinyl)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 294622-82-5 CAPLUS
CN Pyridinium, 3-[4-[4-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]-1-methyl-, iodide (1:1) (CA INDEX NAME)

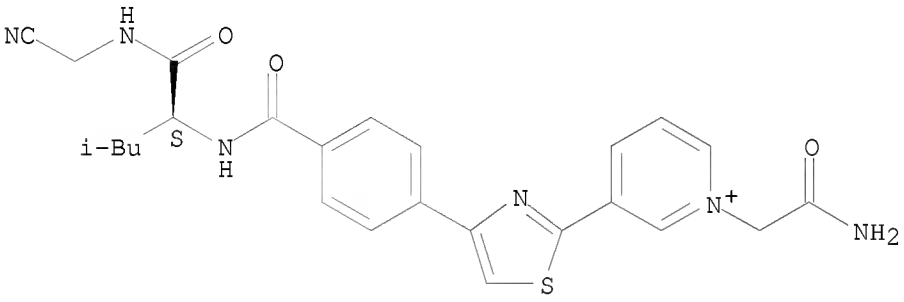
Absolute stereochemistry.



● I^-

RN 294622-83-6 CAPLUS
CN Pyridinium, 1-(2-amino-2-oxoethyl)-3-[4-[4-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]-, bromide (1:1) (CA INDEX NAME)

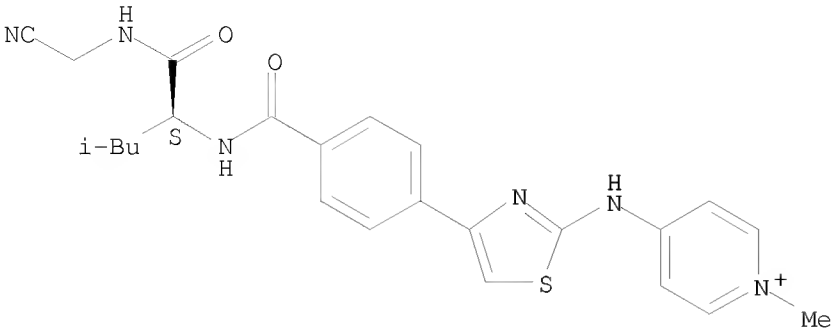
Absolute stereochemistry.



● Br^-

RN 294622-84-7 CAPLUS
CN Pyridinium, 4-[[4-[4-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]amino]-1-methyl-, iodide (1:1) (CA INDEX NAME)

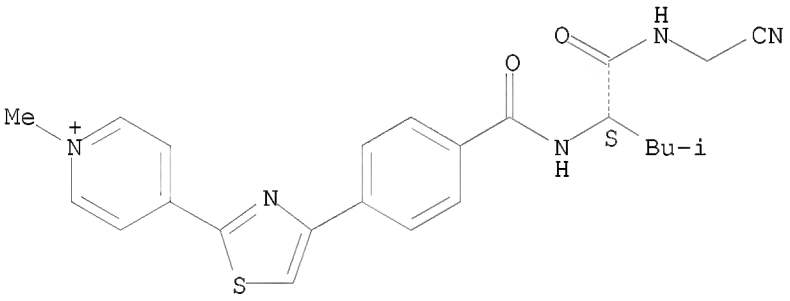
Absolute stereochemistry.



● I^-

RN 294622-85-8 CAPLUS
CN Pyridinium, 4-[4-[4-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]-1-methyl-, iodide (1:1) (CA INDEX NAME)

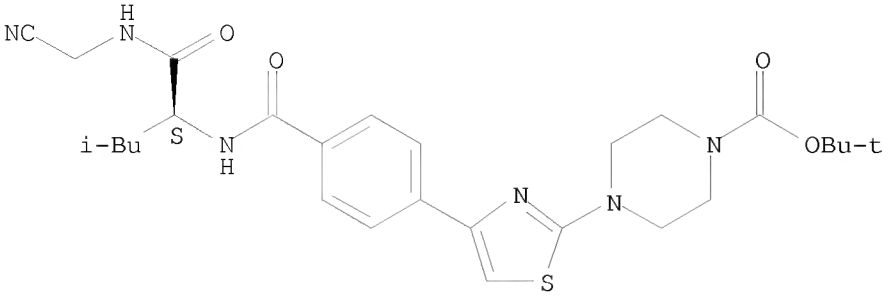
Absolute stereochemistry.



● I^-

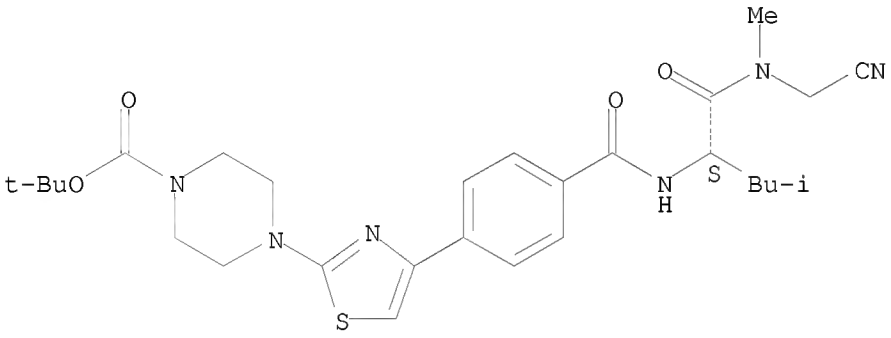
RN 294622-89-2 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-[4-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)

Absolute stereochemistry.



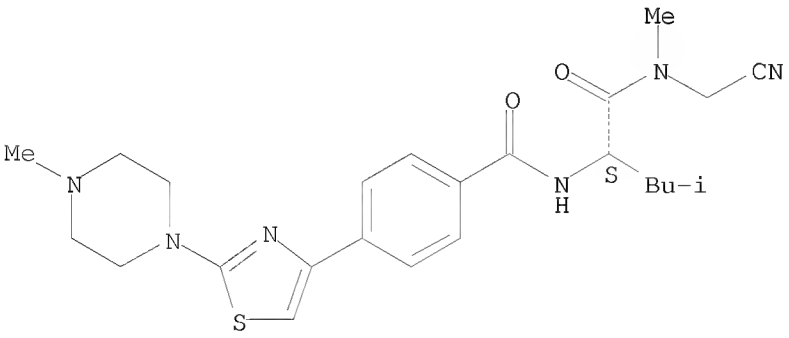
RN 294622-95-0 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-[4-[[[(1S)-1-[[(cyanomethyl)methylamino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)

Absolute stereochemistry.



RN 294622-96-1 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)methylamino]carbonyl]-3-methylbutyl]-4-[2-(4-methyl-1-piperazinyl)-4-thiazolyl]- (CA INDEX NAME)

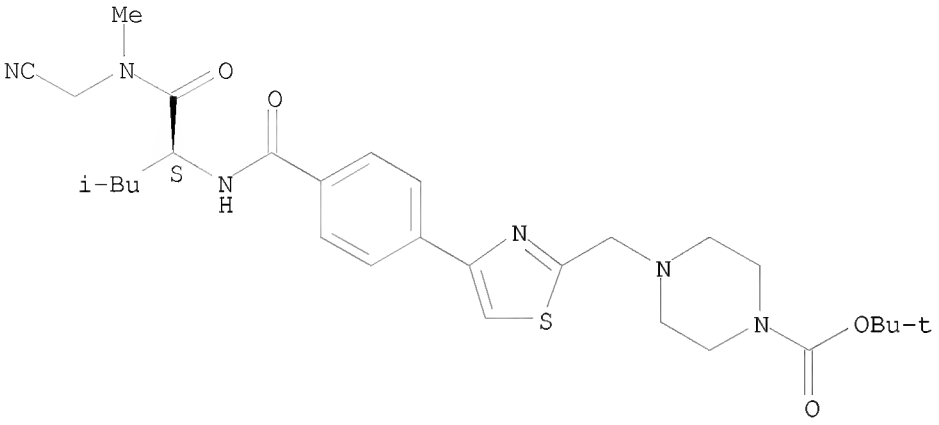
Absolute stereochemistry.



RN 294622-97-2 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[4-[4-[[[(1S)-1-

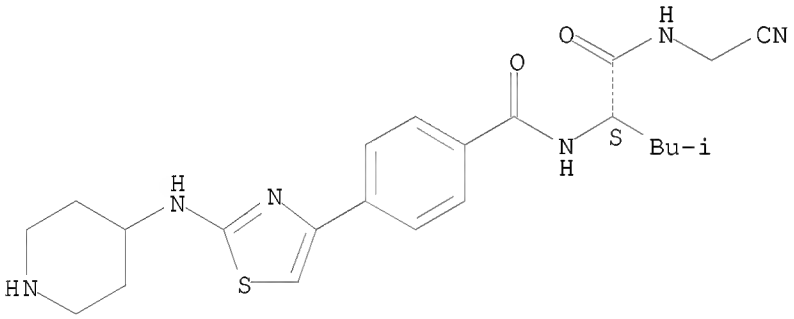
[[(cyanomethyl)methylamino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]methyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)

Absolute stereochemistry.



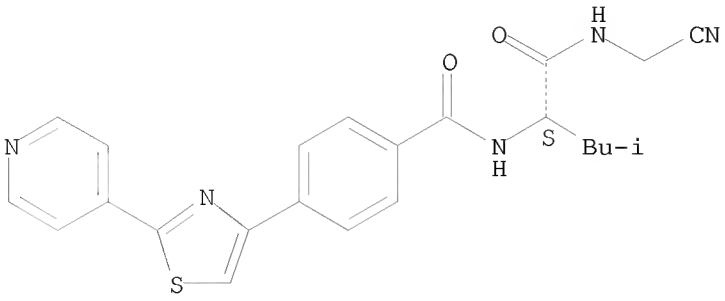
RN 294623-00-0 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[2-(4-piperidinylamino)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



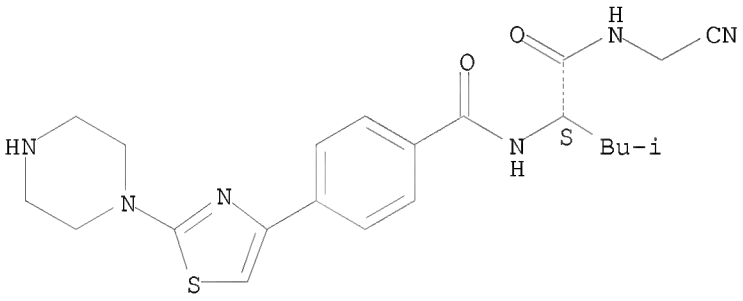
RN 294623-02-2 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[2-(4-pyridinyl)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



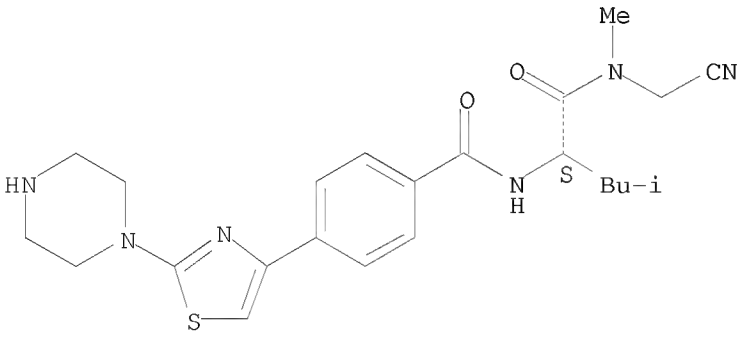
RN 294623-03-3 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[2-(1-piperazinyl)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



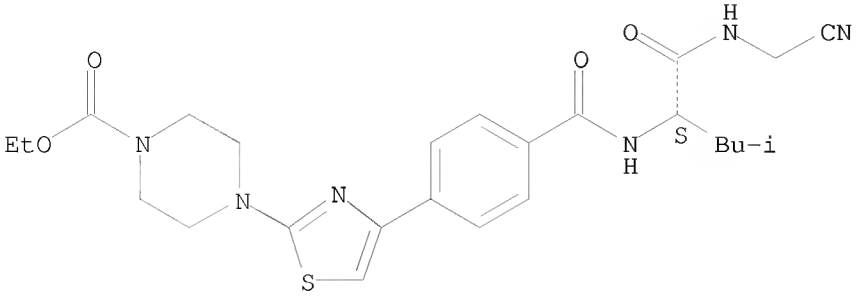
RN 294623-08-8 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)methylamino]carbonyl]-3-methylbutyl]-4-[2-(1-piperazinyl)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.

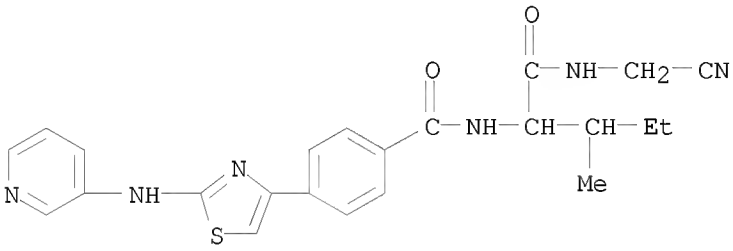


RN 294623-11-3 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-[4-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]-, ethyl ester (CA INDEX NAME)

Absolute stereochemistry.

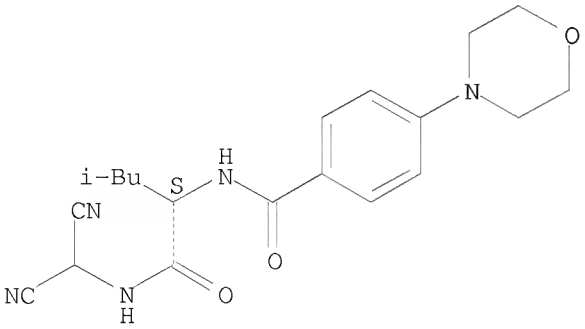


RN 294623-34-0 CAPLUS
CN Benzamide, N-[1-[[(cyanomethyl)amino]carbonyl]-2-methylbutyl]-4-[2-(3-pyridinylamino)-4-thiazolyl]- (CA INDEX NAME)

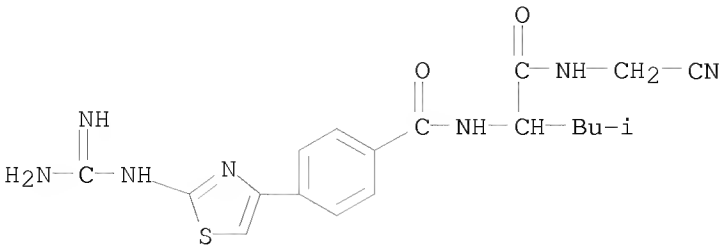


RN 294623-40-8 CAPLUS
CN Benzamide, N-[(1S)-1-[[(dicyanomethyl)amino]carbonyl]-3-methylbutyl]-4-(4-morpholinyl)- (CA INDEX NAME)

Absolute stereochemistry.

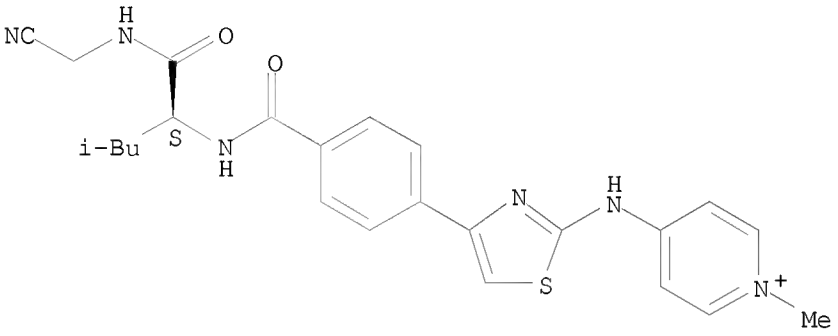


RN 294623-42-0 CAPLUS
CN Benzamide, 4-[2-[(aminoiminomethyl)amino]-4-thiazolyl]-N-[1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]- (CA INDEX NAME)



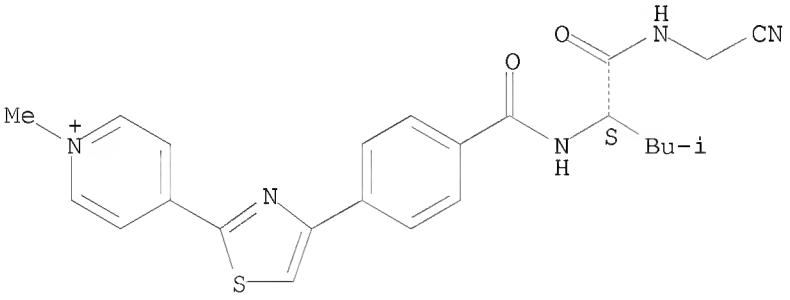
RN 294623-44-2 CAPLUS
CN Pyridinium, 4-[[4-[4-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]amino]-1-methyl- (CA INDEX NAME)

Absolute stereochemistry.



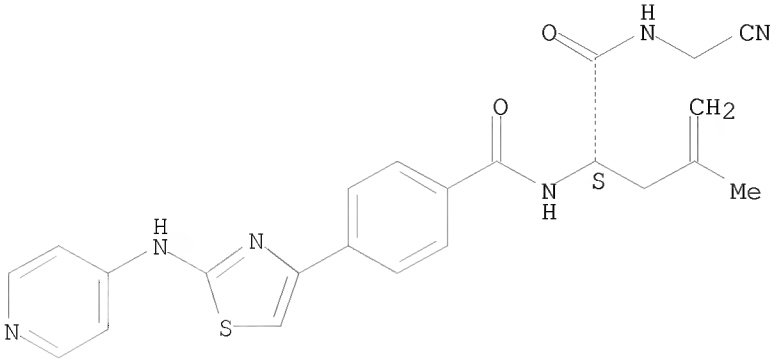
RN 294623-45-3 CAPLUS
CN Pyridinium, 4-[4-[4-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]-1-methyl- (CA INDEX NAME)

Absolute stereochemistry.



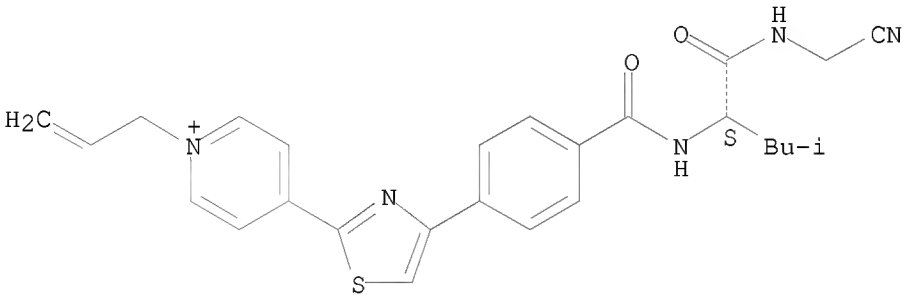
RN 294623-46-4 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methyl-3-buten-1-yl]-4-[2-(4-pyridinylamino)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



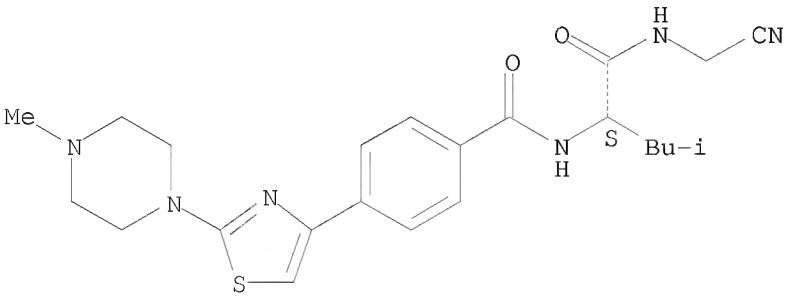
RN 294623-47-5 CAPLUS
CN Pyridinium, 4-[4-[4-[[[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]amino]carbonyl]phenyl]-2-thiazolyl]-1-(2-propen-1-yl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 294623-48-6 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-[2-(4-methyl-1-piperazinyl)-4-thiazolyl]- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 37 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:666700 CAPLUS
DOCUMENT NUMBER: 133:252170

TITLE: Preparation of novel N-cyanomethyl amides as protease inhibitors
INVENTOR(S): Bryant, Clifford M.; Bunin, Barry A.; Kraynack, Erica A.; Patterson, John W.
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000055125	A2	20000921	WO 2000-US6747	20000315
WO 2000055125	A3	20010426		
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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BR 2000009042	A	20011226	BR 2000-9042	20000315
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HU 2002000503	A2	20020629	HU 2002-503	20000315
HU 2002000503	A3	20050628		
US 6455502	B1	20020924	US 2000-526090	20000315
TR 200201874	T2	20021021	TR 2002-1874	20000315
US 6476026	B1	20021105	US 2000-526485	20000315
JP 2002539191	T	20021119	JP 2000-605556	20000315
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NZ 514234	A	20040227	NZ 2000-514234	20000315
AT 259782	T	20040315	AT 2000-916343	20000315
AU 774827	B2	20040708	AU 2000-37461	20000315
PT 1178958	T	20040730	PT 2000-916343	20000315
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ES 2245303	T3	20060101	ES 2000-916375	20000315
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NO 2001004485	A	20011105	NO 2001-4485	20010914

IN 2001KN00949	A	20050311	IN 2001-KN949		20010914
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US 20020086996	A1	20020704	US 2001-17851		20011214
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US 20030119788	A1	20030626	US 2002-241001		20020909
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			US 2000-526090	A1	20000315
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			WO 2000-US6747	W	20000315
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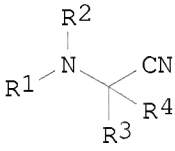
OTHER SOURCE(S): MARPAT 133:252170

GI



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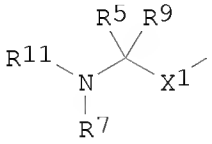

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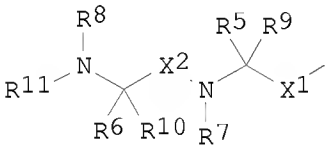

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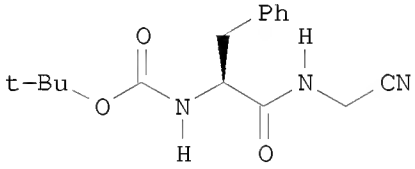


IV

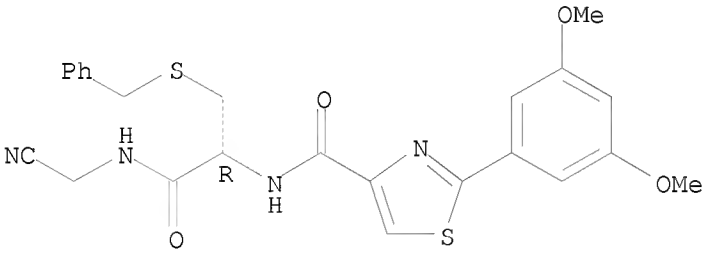
AB The title compds. [I; R1 = II, III (wherein X1, X2 = CO, CH2SO2; R5, R6 = H, alkyl; R7, R8 = H, alkyl, etc.; R9, R10 = alkyl optionally substituted with CN, halo, NO2, etc.; R11 = X5X6R18; X5 = CO, COCO, SO2; X6 = a bond, O, NH, N(alkyl); R18 = alkyl optionally substituted with CN, halo, NO2, etc.); R2 = H, alkyl, etc.; R3 = H, alkyl, etc.; R4 = H, alkyl optionally substituted with CN, halo, NO2, etc.; R4 and R2 taken together form trimethylene, tetramethylene, phenylene-1,2-dimethylene, optionally substituted with hydroxy, oxo or methylene; R4 and R3 together with the carbon atom to which both are attached form cycloalkylene, heterocycloalkylene], useful for treating diseases associated with cysteine protease activity, particularly diseases associated with activity of cathepsins B, K, L or S such as inflammation and asthma, were prepared and formulated. Thus, reacting 2(S)-tert-butoxycarbonylamino-3-phenylpropionic acid with aminoacetonitrile.HCl in the presence of Et3N in DMF and MeCN afforded the amide (1S)-IV. Biol. data for compds. I were given.

IT 294640-33-8P 294640-34-9P 294641-14-8P

294641-34-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel N-cyanomethyl amides as protease inhibitors)

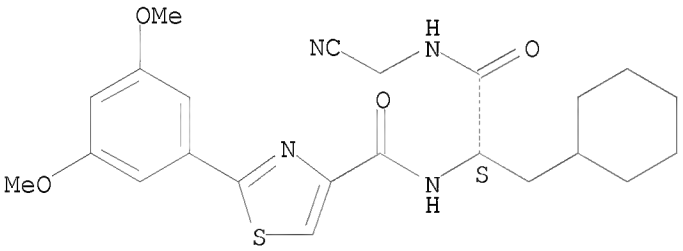
RN 294640-33-8 CAPLUS
CN 4-Thiazolecarboxamide, N-[(1R)-2-[(cyanomethyl)amino]-2-oxo-1-[[(phenylmethyl)thio]methyl]ethyl]-2-(3,5-dimethoxyphenyl)- (CA INDEX NAME)

Absolute stereochemistry.



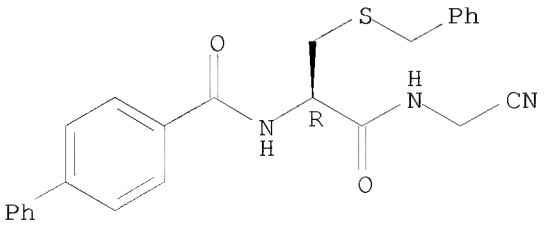
RN 294640-34-9 CAPLUS
CN 4-Thiazolecarboxamide, N-[(1S)-2-[(cyanomethyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]-2-(3,5-dimethoxyphenyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 294641-14-8 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[(1R)-2-[(cyanomethyl)amino]-2-oxo-1-[[(phenylmethyl)thio]methyl]ethyl]- (CA INDEX NAME)

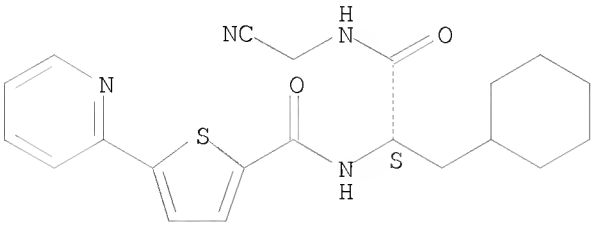
Absolute stereochemistry.



RN 294641-34-2 CAPLUS

CN 2-Thiophenecarboxamide, N-[(1S)-2-[(cyanomethyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]-5-(2-pyridinyl)- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 38 OF 38 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:325961 CAPLUS
DOCUMENT NUMBER: 130:352553
TITLE: Synthesis of dipeptide nitriles as inhibitors of cysteine cathepsins
INVENTOR(S): Altmann, Eva; Betschart, Claudia; Gohda, Keigo; Horiuchi, Miyuki; Lattmann, Rene; Missbach, Martin; Sakaki, Junichi; Takai, Michihiro; Teno, Naoki; Cowen, Scott Douglas; Greenspan, Paul David; McQuire, Leslie Wighton; Tommasi, Ruben Alberto; Van Duzer, John Henry
PATENT ASSIGNEE(S): Novartis AG, Switz.; Novartis-Erfindungen Verwaltungsgesellschaft mbH
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9924460	A2	19990520	WO 1998-EP6937	19981103
WO 9924460	A3	19990902		
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RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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AU 9914873	A	19990531	AU 1999-14873	19981103
AU 751669	B2	20020822		
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TR 200001189	T2	20000921	TR 2000-1189	19981103
JP 2001522862	T	20011120	JP 2000-520468	19981103
HU 2000004400	A2	20020429	HU 2000-4400	19981103

RU 2201420	C2	20030327	RU 2000-114821		19981103
CN 1273444	C	20060906	CN 1998-810768		19981103
ZA 9810073	A	19990505	ZA 1998-10073		19981104
TW 527362	B	20030411	TW 1998-87118553		19981105
NO 2000002320	A	20000704	NO 2000-2320		20000502
MX 2000PA04375	A	20001211	MX 2000-PA4375		20000504
US 6353017	B1	20020305	US 2000-643639		20000822
US 20040029814	A1	20040212	US 2003-342872		20030115
US 20040110806	A1	20040610	US 2003-694672		20031028
US 20060235220	A1	20061019	US 2006-374995		20060315
US 20080027060	A1	20080131	US 2007-835134		20070807
PRIORITY APPLN. INFO.:			GB 1997-23407	A	19971105
			US 1997-108160P	P	19971205
			US 1997-985973	A	19971205
			WO 1998-EP6937	W	19981103
			US 1998-186223	B1	19981104
			US 2000-643639	A1	20000822
			US 2002-54590	B1	20020122
			US 2003-342872	A1	20030115
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			US 2006-374995	B1	20060315

OTHER SOURCE(S): MARPAT 130:352553

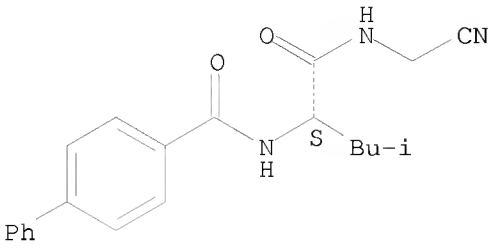
AB N-terminal substituted dipeptide nitriles R(L)xX1NHCR2R3C(:Y)NHCR4R5CN [R is optionally substituted aryl, alkyl, alkenyl, alkynyl, heterocyclyl; R2, R3 = H, optionally substituted alkyl, cycloalkyl, bicycloalkyl, or aryl-, biaryl-, cycloalkyl, bicycloalkylalkyl; R2 and R3 together represent alkylene, optionally interrupted by O, S, or NR6, where R6 is H, alkyl, arylalkyl; or R2 or R3 are linked by alkylene to the adjacent nitrogen to form a ring; R4, R5 = H, optionally substituted alkyl, arylalkyl, CO2R7, CONR7R8 (R7 is optionally substituted alkyl, aryl, arylalkyl, cycloalkyl, bicycloalkyl, or heterocyclyl and R8 is H or optionally substituted alkyl, aryl, arylalkyl, cycloalkyl, bicycloalkyl, heterocyclyl), etc.; R4 and R5 together represent alkylene, optionally interrupted by O, S, or NR6; X1 = CO, CS, SO, SO2, P(O)OR6; Y = O, S: L is optionally substituted Het, Het-CH2, CH2-Het (Het = O, N, or S); x = zero or 1] were prepared as inhibitors of cysteine cathepsins, e.g., cathepsins B, K, L and S, and can be used for the treatment of cysteine cathepsin dependent diseases and conditions. Thus, N-[2-[(3-carboxyphenyl)methoxy]-1(S)-cyanoethyl]-3-methyl-Nα-(2,2-diphenylacetyl)-L-phenylalaninamide was prepared and shown to have IC50 ≈ 5 nM for inhibition of cathepsin B.

IT 225118-29-6P 225118-35-4P 225118-36-5P
225119-22-2P 225119-24-4P 225119-30-2P
225119-32-4P 225119-33-5P 225119-37-9P
225119-42-6P 225120-10-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of dipeptide nitriles as inhibitors of cysteine cathepsins)

RN 225118-29-6 CAPLUS

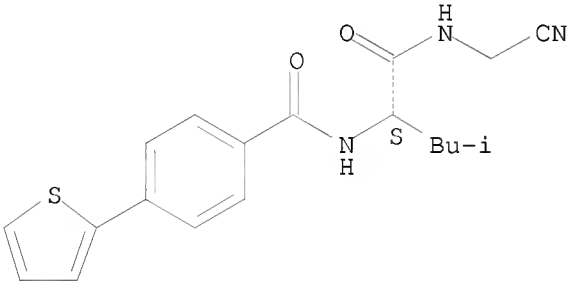
CN [1,1'-Biphenyl]-4-carboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]- (CA INDEX NAME)

Absolute stereochemistry.



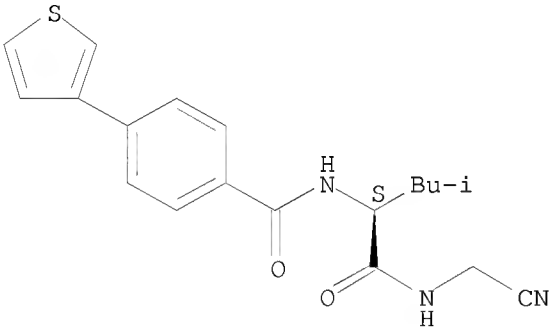
RN 225118-35-4 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-(2-thienyl)- (CA INDEX NAME)

Absolute stereochemistry.



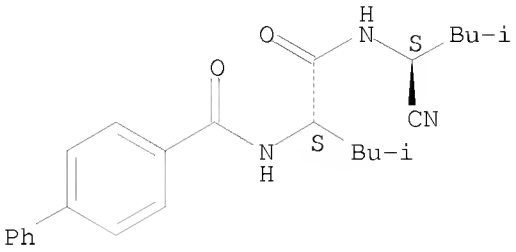
RN 225118-36-5 CAPLUS
CN Benzamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-4-(3-thienyl)- (CA INDEX NAME)

Absolute stereochemistry.



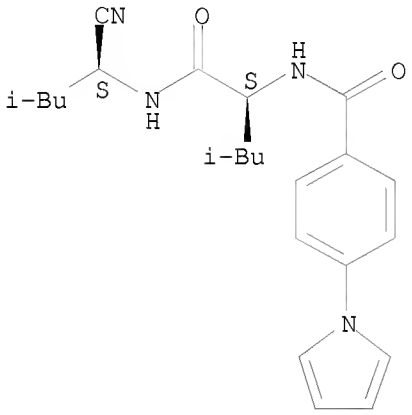
RN 225119-22-2 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]-3-methylbutyl]- (CA INDEX NAME)

Absolute stereochemistry.



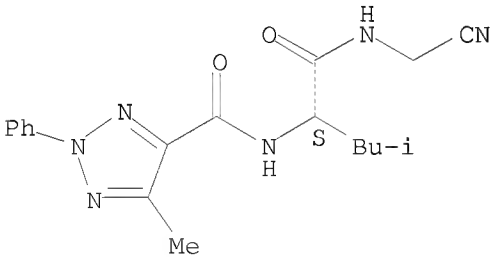
RN 225119-24-4 CAPLUS
CN Benzamide, N-[(1S)-1-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]-3-methylbutyl]-4-(1H-pyrrol-1-yl)- (CA INDEX NAME)

Absolute stereochemistry.



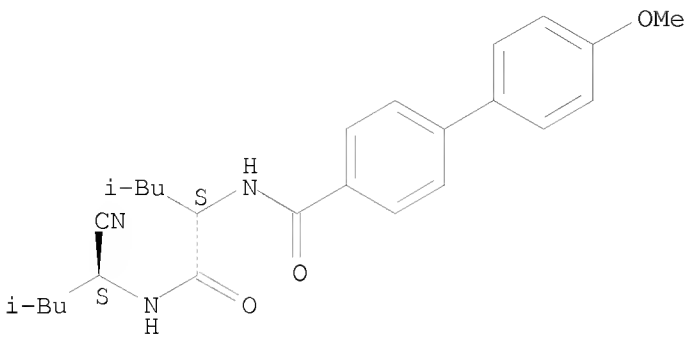
RN 225119-30-2 CAPLUS
CN 2H-1,2,3-Triazole-4-carboxamide, N-[(1S)-1-[[(cyanomethyl)amino]carbonyl]-3-methylbutyl]-5-methyl-2-phenyl- (CA INDEX NAME)

Absolute stereochemistry.



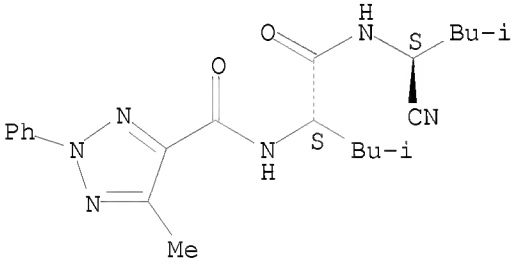
RN 225119-32-4 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]-3-methylbutyl]-4'-methoxy- (CA INDEX NAME)

Absolute stereochemistry.



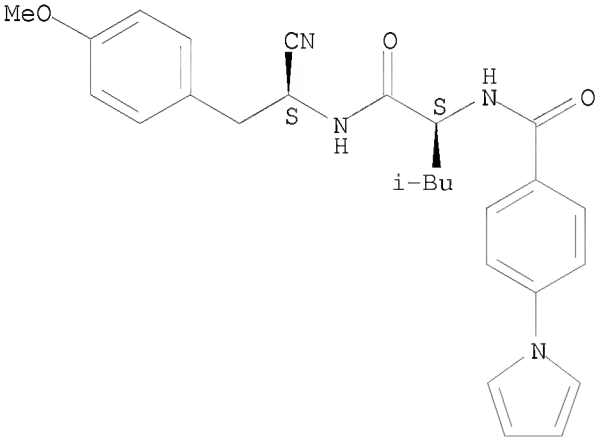
RN 225119-33-5 CAPLUS
CN 2H-1,2,3-Triazole-4-carboxamide, N-[(1S)-1-[[[(1S)-1-cyano-3-methylbutyl]amino]carbonyl]-3-methylbutyl]-5-methyl-2-phenyl- (CA INDEX NAME)

Absolute stereochemistry.



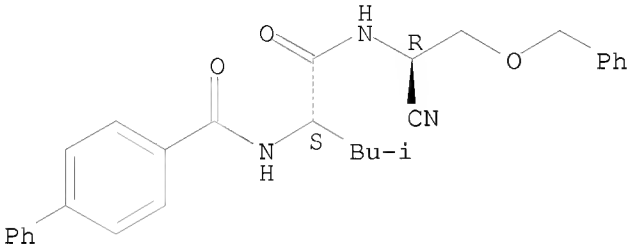
RN 225119-37-9 CAPLUS
CN Benzamide, N-[(1S)-1-[[[(1S)-1-cyano-2-(4-methoxyphenyl)ethyl]amino]carbonyl]-3-methylbutyl]-4-(1H-pyrrol-1-yl)- (CA INDEX NAME)

Absolute stereochemistry.



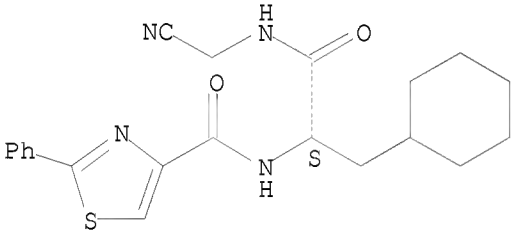
RN 225119-42-6 CAPLUS
CN [1,1'-Biphenyl]-4-carboxamide, N-[(1S)-1-[[[(1R)-1-cyano-2-(phenylmethoxy)ethyl]amino]carbonyl]-3-methylbutyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 225120-10-5 CAPLUS
CN 4-Thiazolecarboxamide, N-[(1S)-2-[(cyanomethyl)amino]-1-(cyclohexylmethyl)-2-oxoethyl]-2-phenyl- (CA INDEX NAME)

Absolute stereochemistry.



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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	209.02	387.59
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-30.40	-30.40

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 17:31:49 ON 21 DEC 2008